Relation between Serum Level of Selenium And Zinc in Children with Dysfunctional Thyroid Disorders

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Abstract:

Zinc (Zn) and selenium (Se) are essential trace elements involved in thyroid hormone metabolism. Aim of this paper is to review the role of micronutrients in thyroid function and diseases.

Keywords: zinc, selenium, supplementation, thyroid function.

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Introduction:

Zinc is one of the essential trace elements. It is the second most abundant trace element in the human body. The human body contains about 2 gm of zinc and approximately 95% of this zinc is found within cells. About 57% of the body pool is stored in skeletal muscles, 29% in bone and 6% in skin but zinc is found in all body tissues and fluids **(1)**.

Zinc plays important roles in growth and development, the immune response, neurological function, and reproduction. On the cellular level, the function of zinc can be divided into three categories: catalytic, structural, and regulatory **(2)**. The structure and function of cell membranes are also affected by zinc. Loss of zinc from biological membranes increases their susceptibility to oxidative damage and impairs their function **(3)**.

Selenium (Se) is an essential trace element having biological functions of utmost importance for human health. Differently from the other (semi)metals, it is incorporated into proteins by a co-translational mechanism as part of the amino acid seleno- cysteine (SeCys). Most Se-proteins participate in antioxidant defence and redox state regulation, particularly the families of glutathione peroxidases (GPxs) and thioredoxin reductases (TrxRs). **(4).**

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Since acute or chronic exposure to heavy metals can have effects on people's health, their monitoring in the human body fluids, such as blood serum, is considered as an indicator. These days, thyroid disorders such as hypothyroidism are very common. A study showed that thyroid gland needs the different nutrients to synthesize its hormones. In this regards, selenium is one of an important factors to metabolize thyroid hormones. Thyroid gland includes high levels of selenium that attach to many selenoproteins and protect the gland from an excess of hydrogen peroxide generated to product the thyroid hormones. **(5).**

In this regards, **Parshukova *et al*. (6)** confirmed that low serum selenium levels have an effect on the thyroid hormone levels in North European Russia. Also, another study in China showed that higher plasma selenium was related to lower chance to be affected by hypothyroidism. Since selenium is not produced in the human body and low access to the selenium may cause abnormalities of thyroid metabolism disorders. It is needed for proper functioning of the immune system and is an important factor in the metabolism of thyroid hormones. (**7**).

Despite the expected relationship between selenium and thyroid function, few studies have revealed the positive influence of selenium supplementation on thyroid hormone levels. Moreover, rare studies in Iran have investigated effects of selenium deficiency in thyroid disorders including pediatrics with acquired hypothyroidism. Therefore, this study aimed to evaluate role of selenium deficiency in children and adolescents with acquired hypothyroidism in southern Iran (**8).**

Two studies from Brazil have shown that selenium level in that region has influenced thyroid function. Also, **Kawai *et al*. (9**) have explained the effect of selenium deficiency on thyroid function. Also, another study conducted in Iraq reported that the plasma selenium level in the hypothyroidism patients were significantly less than the healthy samples. On the contrary, **Jang *et al*. (10**) who evaluated hypothyroidism patients in Korea, have found that selenium deficiency isn't a common result amongst these patients.

Some studies have also been conducted in Iran. **Nazemi *et al*. (11)** revealed that selenium level of water and soil was low in different regions of our country. Moreover, another study showed that administration of selenium to hypothyroidism women leads to thyroid function improvement. But, study by **Nourbakhsh *et al*. (12)** revealed that there was no difference in selenium and selenoprotein levels among hypothyroidism and healthy children and adolescents. The diversity of geographical and environmental factors can be the reason why Iranian researchers have different findings regarding the role of selenium in thyroid disorders.

The lowest serum selenium levels in healthy Iranian children have been reported in the study of **Mahyar *et al*. (13**) In Qazvin and the study of **Amiri *et al*. (14**) and the highest serum selenium levels was in the study of **Khoshdel *et al*. (15**) from Shahrekord, *Iran*. Differences in studies can be related to differences in type of nutrition and geographical location, and possibly factors such as age, gender, diet, and the amount of selenium in different areas. Also, enzymatic changes, increased free radicals and ultimately neurological disorders are other factors that can have an effect on the selenium levels. (**16**) According to controversy the selenium level in different Iranian studies, it is recommended that selenium levels be assessed in the different age groups of children across the country as a national plan.

Zinc is a trace element that plays a role in cell proliferation and biochemical reactions in the body. Moreover, the thyroid is considered to have an important role in zinc hemostasis. The association between zinc and thyroid metabolism is based on the hypothesis that the nuclear T3 receptor contains zinc-binding protein. Thus, thyroid hormones have an effect on zinc absorption and excretion. The role of copper in thyroid tissue is yet unclear. Moreover, as per data, it has been shown that inadequate or excessive uptake may affect thyroid hormone metabolism. Copper and zinc are well-known components of antioxidant defense. They serve as cofactors of some proteins in the modification of transcription factors and receptors in the regulation of critical cellular processes hence, these trace elements may lead to various pathophysiological consequences depending on the amount (**17).**

Abnormalities in iodine and selenium intake may cause thyroid dysfunction and structural changes in the thyroid gland. Due to moderate iodine deficiency, salt iodization has been mandatory since 1998 as a public health strategy (**18**) in Turkey. Despite the salt iodization, iodine deficiency continues in some regions in Turkey. However, according to a study conducted in 2007, iodine deficiency is not common in Yozgat. (**19**) After salt iodization, iodine screening between 2002 and 2007 showed that the median urinary iodine concentration increased from 56 μg/L to 116 μg/L. (**20)** According to these data, there is no significant iodine deficiency in Yozgat. Since the effect of selenium and iodine on the thyroid is interrelated, this provides a relatively safe basis for the study.

It has been reported that iodine deficiency and severe selenium may cause an increase in TSH levels and/or thyroid volume. In Denmark, **Rasmussen *et al*. (21)** reported that low serum selenium concentration was associated with a higher risk for an enlarged thyroid gland and for the development of thyroid nodules. In a study by **Derumeaux *et al*., (22**) there was no increased risk of thyroid nodules in patients with low serum selenium. In the study with 6152 participants in China; 3038 individuals were included in the area containing sufficient selenium and 3114 persons were included in the area containing low selenium and the prevalence of thyroid diseases among the regions was evaluated. The prevalence of thyroid diseases including hypothyroidism, subclinical hypothyroidism, autoimmune thyroiditis, and diffuse goiter was higher in the group involved in the lower selenium-containing region. This study is a multi-participatory study but the effect of thyroid hormones and autoimmunity diseases on selenium cannot be distinguished. We selected the patient and the control group from euthyroid status and negative thyroid antibodies so that selenium was not affected by other factors. In our study, selenium levels were significantly lower in patients with nodular goiter. As reported in previous studies, selenium deficiency is associated with a higher prevalence of thyroid disease. Hence, further data are required to prove that selenium has a protective effect against nodular goiter. (**7).**

The relationship between low serum selenium level and cancer is an important research topic. In a meta-analysis of 1291 patients, **Shen *et al*. (23**) investigated the relation of serum selenium and copper levels with thyroid cancers. They concluded that patients with thyroid cancer had lower serum selenium and higher copper levels than healthy controls. **Jonklaas *et al*. (24)** evaluated 65 euthyroid patients undergoing thyroidectomy for thyroid cancer, suspected thyroid cancer, or nodular goiter and demonstrated a potential relationship between low selenium concentrations and high thyroid cancer grade. This data suggests that the antioxidant properties of selenoenzymes in which selenium is involved are related to carcinogenesis and tumor progression.

Zinc is one of the trace elements in the human body. The relationship of this element with thyroid is that the thyroid hormone binding transcription factors involved in gene expression contain zinc. (**25)** A study reported that free T4 and T3 levels were significantly lower in patients with goiter and zinc deficiency. (**26**) Besides, serum zinc levels were reported to be low in hypothyroidism and high in hyperthyroidism (**27**) whereas **Nishi *et al*. (28**) reported that serum zinc levels were similar between the patients with hypothyroidism and the control group. **Giray *et al*. (29**) did not find a significant difference in the zinc levels between nodular goiter and controls. Our data showed that low zinc levels were associated with euthyroid nodular goiter but they were not associated with solitary or multiple nodular goiter. Zinc deficiency can play a significant role in the development of goiter nevertheless, different factors may play a role in the nodule increase.

Copper plays a role in both antioxidant and prooxidant events in the body. The data about the relationship between serum copper level and thyroid disease is conflicting. A study with rats showed a relation between copper deficiency and low plasma T3 level. **Giray *et al*.,(30**) **Kazi *et al*.,(31**) and **(32)** reported that the serum copper level was lower in patients with nodular goiter compared to the control group whereas, in another study, the postoperative copper level of the patients with benign nodular gland was reported to be lower than the preoperative copper level. In our study, no significant difference was found between the groups with respect to copper levels.

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