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Iodine and Zinc, But Not Selenium and Copper, Deficiency Exists in a Male Turkish Population with Endemic Goiter

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ABSTRACT

Although endemic goiter has been shown to have a high prevalence in Turkey, little is known about the concentration of urinary iodine, plasma selenium (Se), copper (Cu), and zinc (Zn) in these patients. We studied on 140 male patient with endemic goiter (mean age: 22.2 ± 0.19 yr) and 140 healthy male subjects (mean age: 21.8 ± 0.28 yr). Daily urinary iodine excretion was determined by the ionometric method. Plasma Se, Zn, and Cu were determined by using atomic absorption spectrometry. Daily urinary iodine excretion was found to be significantly lower in the patient group (38.7 ± 2.26 μg/d) than that of controls (50.73 ± 2.56 μg/day, p = 0.001). Plasma Zn concentrations were also found to be significantly lower in the patient group (1.04 ± 0.03 μg/mL) than that of controls (1.16 ± 0.02 μg/mL, p = 0.001). No significant difference was determined in Se and Cu concentrations between the patient and control groups. Our study shows that a moderate iodine deficiency exists in both patients with endemic goiter and control subjects, which indicates the important role of iodine deficiency in the etiopathogenesis of endemic goiter in Turkey. Zinc deficiency may also contribute to the pathogenesis of endemic goiter. However, Se and Cu do not seem to have any role in the

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etiopathogenesis of endemic goiter in Turkey. A community-based iodine fortification program throughout the country may be proposed to take over the problem, which also can prevent the contributing effects of other element deficiencies that occur when iodine deficiency is the prevailing factor.

Index Entries: Endemic goiter; iodine; zinc; selenium; copper; Turkey.

INTRODUCTION

Endemic goiter has been reported to have high prevalences varying from 9.2% to 30.5% in Turkey. Kologlu and Kologlu *(1)* measured the iodine content of the drinking water in 72 different provinces in the Black Sea region of Turkey and demonstrated low iodine content (0–0.25 μg/L). They also showed that foodstuff in this region contains low iodine, which makes 55–75 μg iodine in a daily diet. The largest epidemiological study was reported in 1987 by Hatemi et al. *(2)*. They found a total goiter prevalence of 30.5% by neck palpation in all ages in different parts of the country. They also demonstrated that 19% of drinking water sources in Turkey contained low iodine. Ozbakir et al. *(3)* recently demonstrated that the prevalence of goiter in the central region of Turkey was 25.8% and the iodine level in drinking water was found to be 3 μg/L. So far, only one study has evaluated daily urinary iodine excretion in the Turkish population *(4)*. This study demonstrated significantly lower urinary iodine concentration in 60 female patients with endemic goiter.

It is well known that selenium (Se) deficiency is also a contributor for endemic goiter *(5,6)*. Moreover, it was reported that zinc (Zn) deficiency may be a stimulus for goitrogenesis in iodine deficiency *(7–9)*. In Zn deficiency, unchanged *(8)* or decreased plasma T3 concentration *(9)* was reported. Furthermore, defects in copper (Cu) metabolism in thyroid dysfunction *(10,11)* and elevated T3 level in rats with Cu deficiency *(12)* was reported. However, no study evaluated Se, Zn, and Cu levels in patients with endemic goiter in Turkey. We have, therefore, determined iodine, Zn, Se, and Cu levels in Turkish patients with endemic goiter to investigate the role of these elements in the etiopathogenesis of endemic goiter in Turkey.

SUBJECTS AND METHODS

One hundred forty male Caucasian patients (mean age: 22.25 ± 0.19 yr) who were referred to our clinic were selected for the study. Patients were selected equally from each region of the country to homogenize the study population. Turkey has 7 different geographical regions and 20 patients were selected from each region. The thyroid gland was examined by palpation and ultrasonography, and thyroid function tests were performed in all patients. Thyroid sintigraphy was also performed in cases with nodular goiter. One hundred forty healthy males were also selected as a control group. Control subjects were also matched for the different regions of the country and age (mean age: 21.81 ± 0.28 yr). Nodular goiter cases were evaluated for malignancy by cytological examination of fine-needle-aspirated material. Positive cases for neoplastic findings were excluded. Patients and controls who have had any radiological procedure with radiocontrast material, those who have the medicine with L-thyroxin, and those who used iodinated salt were excluded.

Twenty-four hour urine samples were collected from all the patients and controls. The volume of each sample was measured. Each was homogenated and a 50-mL urine samples were obtained in separate plastic tubes. They were kept in a deep freezer at –20°C. Urinary iodide concentrations were measured with an iodide-selective electrode (Orion, 920 A Ionmeter, Orion, 9453 Iodide-selective electrode, and Orion, 900200 Reference electrode, Boston, MA, USA). *(13)* One milliliter of total ionic strength adjuster (Orion, 940011, Boston, MA, USA) was added to 50 mL of urine sample. Iodide determination in urine samples was determined by direct measurement according to the manufacturer's instructions. Standard solutions were prepared by serial dilution of the iodide standard solution (Orion, USA) with distilled deionized water to 1.5, 3.0, 4.5, and 6.0 ppm. Iodide concentrations for each case was expressed as microgram of iodide per day.

Copper, Zn, and Se were measured in venous plasma samples obtained from the patient and control cases at the time of urine collection. Measurements were performed by atomic absorption spectrometry apparatus (Varian, 30/40, Mulgrave, Victoria, Australia). Cu and Zn was determined by flame atomic absorption spectrometry. Se was determined by furnace atomic absorption spectrometry *(14,15)*.

Statistical analyses were performed by using the Student's *t*-test and the Pearson correlation coefficient.

RESULTS

As shown in Table 1, free T3 levels are significantly higher in the patient group when compared to those of the control group, whereas free T4 levels are significantly lower in the patient group when compared to the control group. Iodine and Zn levels were also significantly lower in the patient group compared to those of the control group. However, there is no significant difference in Cu and Se levels between the two groups.

As shown in Table 2, there is no correlation between thyroid function tests and the I, Se, Cu, and Zn levels.

Table 1
Comparison of the Parameters of Patient and Control Groups

Parameter	Patient Group	Control Group	P
Age (yr)	22.25±0.19	21.81±0.28	N.S.
TSH (μIU/ml)	0.83±0.07	0.75±0.06	N.S.
T_3 (pg/ml)	3.42±0.05	3.15±0.09	0.009
T_4 (ng/dl)	1.26±0.04	1.64±0.04	0.001
I (μg/day)	38.75±2.26	50.73±2.56	0.001
Se (ng/ml)	69.68±1.26	71.11±1.74	N.S.
Cu (μg/ml)	0.83±0.02	0.82±0.02	N.S.
Zn (μg/ml)	1.04±0.03	1.16±0.02	0.001

Note: Values are mean ± SEM. $p < 0.05$, significantly different from the control. N.S. = Nonsignificant ($p > 0.05$).

Table 2
Correlation Coefficients Between Parameters

	TSH	T3	T4
I	r= 0.04	r= 0.13	r= 0.08
	P= 0.7	P= 0.3	P= 0.5
Se	r= 0.12	r= 0.12	r= 0.04
	P= 0.3	P= 0.25	P= 0.6
Cu	r= 0.11	r= 0.03	r= 0.01
	P= 0.2	P= 0.8	P= 0.9
Zn	r=0.17	r=0.10	r=0.09
	P=0.2	P= 0.4	P= 0.5

DISCUSSION

Kologlu and Kologlu studied the etiopathogenesis of goiter in the Black Sea region in Turkey *(1)*. Most of the drinking water samples obtained in the region from 72 sources were shown to have low iodine concentrations (0–0.25 μg/L). Control samples from Istanbul had higher iodine concentrations (11 μg/L). They also showed that foodstuff in the region contained low iodine concentrations, which make 55–75 μg iodine in a daily diet *(1)*. The largest epidemiological study was reported in 1987 by Hatemi et al. *(2)*. They also demonstrated that 19% of the sources of drinking water in Turkey had contained low iodine concentrations. They also reported a total goiter prevalence of 30.5% by neck palpation in all ages in different parts of the country *(2)*. However, only one study has already been reported on daily urinary iodine excretion in patients with endemic goiter in Turkey *(4)*. The authors, supporting our findings, determined significantly lower urinary iodine concentrations in 60 female euthyroid goiter patients than that of 20 healthy controls. In this study, urinary iodine concentrations in endemic goiter patients were significantly lower than that of controls. Our results demonstrate a moderate iodine deficiency, which is confirmed by the previous studies reporting prevalence of goiter around 30%.

Another trace element that is essential to thyroid hormone production is selenium. Selenium is an essential constituent of the enzymes glutathione peroxidase (GSH-Px) and type I iothyronine 5′-deiodinase (5′ D-I). Selenium in the form of 5′ D-I is responsible for bioactivating the prohormone thyroxine by converting it to T_3 in peripheral tissues like liver and kidneys and in the thyroid gland itself *(16,17)*. A lack of GSH-Px in the thyroid could involve a decrease of the defense mechanism against hydrogen peroxide (H_2O_2) and an increased cytotoxity, resulting in an involution of the thyroid functional capacity characteristic of endemic myxedematous cretinism. The goiter endemia of Central Africa presents the peculiar feature that most of the cretins in the area are of the myxoedematous type *(18)*. Thiocyanate overload and selenium deficiency have been identified as cofactors of iodine deficiency in influencing the thyroid function. Selenium deficiency mitigates hypothyroxinemia in iodine-deficient subjects *(19)*. However, Se has not been studied for its role in goitrogenesis in Turkey yet. In previous studies, plasma Se concentrations in healthy subjects ranged from 70.849 ± 12.868 to 74.622 ± 8.6 ng/mL *(20–22)*. We found an average of 71.11 ± 16 ng/mL plasma Se concentration in our control subjects and the difference was not significant when compared with our patient-group data (69.68 ± 12.9 ng/mL). Therefore, Se seems not to have any role in goitrogenesis in Turkey.

The relationship between goiter and zinc in Turkey has not been studied yet. In this study, we have determined significantly lower Zn levels in the patient group. These data suggest that in the presence of inadequate iodine supply, Zn deficiency may be a stimulus for the development of goiter.

Our study shows a moderate iodine deficiency in Turkey in both the euthyroid goiter and the control groups. Urinary iodine concentration was significantly low in the patient group and seems to be the reason for endemic goiter. Cu and Se levels do not differ significantly in the patient and control groups. The Zn level is significantly lower in the patient group and may be a contributory factor in goitrogenesis. A community-based iodine fortification program throughout the country may be proposed to take over the problem, which also can prevent the contributing effects of other element deficiencies that occur when iodine deficiency is the prevailing factor.

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