



Iodine, copper, zinc, selenium and molybdenum levels in children aged between 6 and 12 years in the rural area with iodine deficiency and in the city center without iodine deficiency in Hatay

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Abstract

Aim: Thyroid diseases related with iodine deficiency are observed commonly in our country and in the world. In this study, we aimed to investigate iodine deficiency in urine and selenium, zinc, copper or molybdenum deficiency which may accompany this in children aged between 6 and 12 years in two schools in the province of Hatay (endemic goitre region).

Material and Methods: This study is a case-control field-study in which students aged between 6 and 12 years were included. One hundred fourteen subjects from the village of Tanışma related to the center of our province and 100 subjects from the city center of Hatay (Antakya) were included in the study. Iodine, selenium, zinc, copper and molybdenum levels were measured in the urine samples of the students included in the study.

Results: Iodine deficiency was found with a severe (5%), moderate (18.4%) and mild degree (43%), respectively in the village of Tanışma. Mild iodine deficiency (7%) was found in the center of Hatay. No moderate and severe iodine deficiency was found in the control group. A significant difference was found between the groups in terms of urine iodine excretion ($p<0.001$). A significant correlation was found between the levels of iodine, selenium, zinc and molybdenum ($p<0.05$). A moderately positive correlation was found between iodine and selenium ($p<0.001$). A moderately positive correlation was found between iodine and zinc levels ($p<0.001$) and a weak correlation was found between iodine and molybdenum ($p<0.01$). No significant correlation was found between iodine level and copper level ($p>0.05$).

Conclusions: Selenium and zinc deficiency may accompany iodine deficiency. Selenium and zinc deficiency should be considered in individuals who are found to have iodine deficiency especially in endemic goitre regions. (Türk Ped Arş 2014; 49: 111-6)

Key words: Endemic goitre, trace elements, iodine deficiency

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Introduction

The main cause of endemic goitre is iodine deficiency (1-4). Iodine is a trace element for thyroid function and its deficiency is the most common cause of preventable mental retardation (4, 5). It is estimated that 2 billion people have iodine deficiency in the world especially in South Asia and Sub-Saharan Africa. It has been reported that iodine deficiency has decreased by 50% in recent years in industrialized countries including Europe, America and Australia (2-4). The most prevalent cause of thyroid diseases in the world is iodine deficiency (6-8). Conclusively, absence of thyroid hormones leads to clinical pictures including goitre, hypothyroidism and hyperthyroidism in newborns and children. The intellectual and motor development of these children are affected negatively (9-11).

In clinically euthyroid cases with iodine deficiency, serum T4 is decreased, thyroid stimulating hormone (TSH) is increased and T3 may be normal or slightly increased. Increased T3 which is metabolically efficient, but requires less iodine is the organism's defense against iodine deficiency. Iodine deficiency causes to increased TSH release in the newborn (12-17).

It has been stated that cognitive and motor functions improve, if mild and moderate iodine deficiency is treated in primary school children (15, 16). If iodine deficiency starts in the embryonic period, health problems including deafness, speechlessness, spastic diplegia, strabismus, severe neurological deficit (neurological cretinism), nanism, psychomotor retardation, stillbirth and mental retardation may be observed (15-18).

Daily iodine requirement is determined to be 150 µg in adolescents and adults, 175-200 µg in pregnant and nursing women, 70-120 µg in children aged between 1 and 10 years and 50 µg below the age of one year (16, 17). The iodine amount excreted by urine constitutes 85-90% of daily iodine intake (2-6). Values below 10 µg/dL in spot urine in school age children indicate insufficient iodine intake (14-17).

Zinc deficiency and selenium deficiency accompanying iodine deficiency have been reported (18, 19). The severity of iodine deficiency in any region can be determined in relation with iodine content of drinking water, the frequency of goitre and urinary iodine excretion rate (7, 10). In this study, we aimed to investigate deficiencies of trace elements including iodine, zinc, molybdenum, copper and selenium and if their urinary excretion rates were related with each other.

Material and Methods

This study was planned by obtaining consent from the patients who were compatible with the Helsinki Declaration

and their relatives with the support of Mustafa Kemal University Scientific Research Project Center and by obtaining permission of the ethics committee (27.05.2010 protocol 2010/11 decision number: 03/14). The study is a case-control study and the target population of the study was consisted of primary school students of Tanışma village found in the rural area of Hatay and primary school students (6-12 years) in the center of Hatay (Antakya). The case group of the study was composed of 114 students who were selected among 700 students studying in Tanışma village primary school. For constitution of the control group, two different schools were selected randomly among the primary schools in Antakya and 100 students were selected from these two schools. The total number of students of these two schools from which the control group was constituted is 3 230. Thus, a total of 214 students were included in the study 100 (46.7%) of whom were from Antakya and 114 (53.3%) of whom were from Tanışma village. The classes were determined randomly in selection of the students who would constitute the case (Tanışma village) and control (Antakya) groups. Afterwards, students were selected from class lists by systematic sampling method. There was no statistically significant difference between the students who were included in the study from Tanışma village and Antakya in terms of gender and age distribution.

Manual thyroid examination was performed in the children who were included in the study. Goitre was graded by two different specialists according to WHO/UNICEF/ICCIDD classification. This classification is as follows: Grade 0: non-palpable goitre. Grade 1: goitre is palpable, but there is no thyroid swelling. Grade 2: swelling can be seen clearly when the neck is in the normal position (20). The urine samples of the students were collected into containers by the investigators with the support of a healthcare worker at school. Urine samples were sent to the laboratory for analysis on the same day. Urine analyses were performed in Ankara in a private laboratory. Water analysis was performed by spectrophotometric study and urinary iodine analysis was performed using Sandell-Koldhoff method. Iodine values in spot urine below 10 µg/dL indicate insufficient iodine intake. If iodine level is below 10 µg/L in water, there is a risk of development of iodine deficiency. Zinc and copper were analysed at a sensitivity of 0.5 mg/L and selenium was analysed at a sensitivity of 10 µg/L using atomic absorption spectrometer (Perkin Elmer Analyst 100) method. Molybdenum was studied at a sensitivity of 0.2 µg/L using ICP-OES (Inductively coupled plasma atomic emission spectroscopy) method. Reference ranges were considered 7-160 µg/L for selenium, 2-80 µg/L for copper, 180-850 µg/L for zinc and 8-34 µg/L for molybdenum. Iodine level was evaluated by Sandell Coldhoff method and a value of <2 µg/dL was considered severe iodine deficiency, a value of 2-5 µg/dL was considered moderate iodine deficiency, a value of 5.1-10 µg/dL was considered mild iodine deficiency, a value of 10.1-20 µg/dL was considered normal, a value of 20.1-30 µg/dL was considered higher than

normal and a value of $>30 \mu\text{g/dL}$ was considered excessive iodine intake (21). Water analyses were performed in the central laboratory of our university.

Statistical analysis

Chi-square test, student's t-test, variance and pearson correlation analyses were used in statistical evaluation (a p value of <0.05 was considered significant). Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) 11.5 statistical software program was used in statistical analysis.

Results

48.6% (104) of 214 students who were included in the study were male and 51.4% (110) were female. The youngest student was 6 years old and the oldest student was 12 years old. 46.7% (100) of the students were from the city center (78 from Bedii Sabuncu primary school and 22 from Vali Ürgen Primary school). 114 students (53.3%) were included in the study from Tanışma village primary school (rural) where iodine deficiency was found before. On manual thyroid examination, goitre was found in 8 students in the rural region and in 2 students in the city center.

In the study group, the lowest urinary iodine level was found to be $0.90 \mu\text{g/dL}$, the highest urinary iodine level was found to be $50.0 \mu\text{g/dL}$ and the mean urinary iodine level was found to be $14.46 \pm 8.9 \mu\text{g/dL}$. The highest, lowest and mean values of selenium, copper, zinc and molybdenum are shown in Table 1. Urinary iodine level was evaluated in Tanışma village and in the center of Hatay separately. In the rural region, the lowest urinary iodine level was found to be $0.90 \mu\text{g/dL}$, the highest urinary iodine level was found to be $31.40 \mu\text{g/dL}$ and the mean urinary iodine level was found to be $9.80 \pm 6.16 \mu\text{g/dL}$, while the same values were found to be $5.60 \mu\text{g/dL}$, $50 \mu\text{g/dL}$ and $19.77 \pm 8.59 \mu\text{g/dL}$, respectively in the center which were significantly lower compared to the rural region ($p < 0.01$).

Iodine level was found to be severely deficient in 1.9% ($n=4$) of the study group, moderately deficient in 9.8% ($n=21$) and slightly deficient in 26.2% ($n=56$). Urinary iodine level was found to be slightly deficient in 64.9% of the subjects in the rural region and in 7% of the subjects in the center; the dif-

ference between the deficiencies was significant ($p < 0.001$) (Table 2).

Compatibility analysis was performed to determine if deficiencies of other trace elements accompanied iodine deficiency in children. A moderate correlation was found between iodine and selenium ($r=0.286$, $p < 0.001$), a moderate correlation was found between iodine and zinc ($r=0.305$, $p < 0.001$) and a mild correlation was found between iodine and molyb-

Table 2. Evaluation of urinary iodine in children aged between 6 and 12 years in the center of Hatay and in Tanışma village

Urinary iodine ($\mu\text{g/dL}$)	Center of Hatay	Acquaintance village	Total	p*
Deficient ($<2.0-10.0$)	7 (7.0%)	74 (64.9%)	81 (87.9)	
Normal ($10.1-20.0$)	54 (54.0%)	30 (26.3%)	84 (39.3%)	<0.001
High ($20.1-30<$)	39 (39.0%)	10 (8.8%)	49 (2.9%)	
Total	100	114	214	

*chi-square test, $X^2=78.86$

Table 3. Relations between urinary iodine, selenium, copper, zinc and molibdenum ($n=214$)

		Selenium	Copper	Zinc	Molibdenum
Iodine	r	0.286	0.131	0.305	0.206
	p	<0.001	0.056	<0.001	<0.01
Selenium	r		0.360	0.408	0.345
	p		<0.001	<0.001	<0.001
Copper	r			0.173	0.171
	p			<0.05	<0.05
Zinc	r				0.340
	p				<0.001

Table 4. Distribution of the mean values of selenium, zinc, molibdenum and copper by urinary iodine levels

Urine	Iodine			p*
	Deficient ($n=81$)	Normal ($n=84$)	High ($n=49$)	
Selenium Mean \pm SD	23.88 \pm 17.46	30.30 \pm 15.04	36.48 \pm 14.16	<0.001
Zinc Mean \pm SD	424.07 \pm 229.78	525.23 \pm 296.46	586.53 \pm 254.89	<0.01
Molibdenum Mean \pm SD	4.79 \pm 4.60	7.26 \pm 5.53	7.37 \pm 5.59	<0.01
Copper Mean \pm SD	9.99 \pm 10.02	10.88 \pm 8.83	14.80 \pm 12.97	<0.01

*Kruskal-Wallis Test. Mean \pm SD: mean \pm standard deviation

Table 1. Iodine, selenium, copper, zinc and molibdenum levels in the urine samples of the students aged between 6 and 12 years by residence in Hatay

	Median	Mean	Minimum	Maximum
Iodine	13.3	14.46	0.9	50
Selenium	28.1	29.29	2.1	81
Copper	8.7	15.45	1.9	65
Zinc	420	500.98	60	1 380
Molibdenum	4.5	6.35	0.1	25

denum ($r=0.206$, $p<0.01$), while no significant correlation was found between iodine and copper ($r=0.131$, $p>0.05$) (Table 3).

When the mean values of selenium, zinc, copper and molybdenum were compared by deficient ($<2-10$ $\mu\text{g/dL}$), normal ($10.1-20$ $\mu\text{g/dL}$) and high ($20.1-30$ $\mu\text{g/dL}$) urinary iodine, significant differences were found between iodine level and the mean values of all other elements (Table 4). However, when detailed Benferonni analysis was performed, no significant differences were found in mean selenium ($p=0.09$), zinc ($p=0.591$) and copper ($p=0.108$) levels between the children with normal iodine levels and the children with high urinary iodine levels.

There was no significant difference between the measurement values of trace elements in the boys and girls. However, zinc and selenium levels in the girls in the city center were significantly lower compared to the boys (zinc; $p=0.02$ and selenium; $p=0.005$). The iodine rate in water was found to be 9.7 $\mu\text{g/dL}$ in the rural regions and 11.2 $\mu\text{g/dL}$ in the city center.

Discussion

It is known that iodine deficiency affects thyroid function and size. In this study, we investigated the urinary iodine level in our region, if deficiency was present and if selenium, zinc, copper and molybdenum deficiencies accompanied iodine deficiency. It was found that selenium, zinc and molybdenum were deficient together with iodine, but urinary copper level was not compatible with iodine level. In a study performed in Sudan, it was reported that the frequency of goitre in this country ranged between 22.2% and 77.7%. While urinary iodine excretion was found to be 2.7 $\mu\text{g/dL}$ in the city of Kosti which is located in the middle part of the country, it was found to be 46.4 $\mu\text{g/dL}$ in Port Sudan on the coast of the red sea (22). In a different study, it was reported that urinary iodine level which was measured by Sandell Kalthoff method in 828 children aged between 4 and 13 years was found to be below 10 $\mu\text{g/dL}$ (iodine deficiency) in 1.9% of the children, $20-30$ $\mu\text{g/dL}$ in 24.6% and above 30 $\mu\text{g/dL}$ in 67.1% (23). According to these results, it can be stated that iodine deficiency rates show variance even in the same country in different regions of the world similar to our study.

In a study in which 444 urinary samples were obtained from school age children in the central and rural regions of Armenia, Tebaida and Caimo, no significant difference could be found between the girls and boys (24). In this study, iodine deficiency was found with a rate of 11% and 18%, respectively. In this iodine deficiency study, it was shown that iodine deficiency was found with a significantly higher rate in individuals with poor economical level (24). Similarly, no difference related with gender was found in terms of iodine deficiency in our study and iodine deficiency was observed with a higher rate in the rural region where the economical level was lower.

In a study performed in Tamil Nadu region, 1230 children aged between 6 and 12 years were examined and the total rate of goitre was found to be 13.5% and the mean urinary iodine excretion was found to be 8.95 $\mu\text{g/dL}$ which was low (25). In our study, the mean urinary iodine excretion was found to be 14.46 ± 8.9 $\mu\text{g/dL}$ which was higher compared to this study and severe iodine deficiency was found in 1.9% of the subjects ($n=4$), moderate iodine deficiency was found in 9.8% of the subjects ($n=21$) and mild iodine deficiency was found in 26.2% of the subjects ($n=56$). Iodine deficiency was found with a higher rate in the rural region compared to the city center. On manual thyroid examination, goitre was found with a rate of 7.02% in the rural region ($n=8$) and with a rate of 0.93% in the city center ($n=2$).

Biological studies have shown that hypothyroidism due to iodine deficiency may be related with selenium (26). In boys and girls with goitre in whom urinary iodine level and plasma selenium level were evaluated, selenium deficiency was reported with a higher rate compared to the ones without goitre (27). In a randomized placebo controlled study, no correlation was found between urinary iodine intensity and plasma selenium intensity (28). In our study, it was found that selenium deficiency accompanied iodine deficiency and there was a positive relation between them when urinary iodine and selenium levels were evaluated.

It has been reported that thyroid hormone level improved 6 months after starting zinc treatment in patients with goitre (29). There are also studies reporting that the frequency of goitre was not related with low or normal level of zinc (30, 31). In a cross-sectional study performed in a mountained region of Iran in 2003, goitre and serum zinc level were investigated. In this study, 828 school-age children were selected by cluster sampling method. Serum zinc level and urinary iodine level were compared and no significant difference was found between the children with and without goitre (31). In our study, zinc deficiency was also found to be statistically significant in the patients in whom iodine deficiency was found. It has been reported that the rate of goitre and thyroid size increase in patients in whom decreased serum selenium is found and they are related with each other (32, 33). In another cross-sectional study, it has been reported that selenium deficiency might protect people from goitre and mild thyroid dysfunction (34). In another study, plasma selenium, zinc and iron levels were not different, while copper and manganese levels were found to be significantly high in patients with multi-nodular goitre. A relation was found between free T3/T4 ratio and plasma copper level as well as iodine (35). In our study, a significant relation was found between urinary selenium level and iodine level. Selenium deficiency also accompanied iodine deficiency and a positive correlation was found between them. However, no significant correlation was found between urinary copper level and iodine level.

Conclusively, we found that selenium and zinc deficiency accompanied iodine deficiency and molybdenum deficiency might also accompany and there was a slightly positive correlation between iodine and molybdenum. We think that trace elements including zinc and selenium should be added to supportive therapy in addition to iodine supportive therapy in patients in whom iodine deficiency is found in endemic goitre regions.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Mustafa Kemal University.

Informed Consent: Written informed consent was obtained from patients and their parents who participated in this study.

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