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Selenium status in Turkey

Possible link between status of selenium, iodine, antioxidant enzymes and oxidative DNA damage

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Measured ($n = 36$, 51 μg/day) and estimated ($n = 274$, 44 μg/day) dietary daily intake of selenium in Turkey is low compared to the RDA value of 55 μg Se/day. When the existence of high prevalence of iodine deficiency in most part of the country is considered, adequate level of dietary Se becomes more important. We have found recently that high iodine-deficient goitrous children had lower Se levels and antioxidant enzyme (AOE) activities, and higher levels of DNA base lesions than non-goitrous controls.

Introduction

Selenium is an essential trace element with fundamental importance for the human biology. It is the constituent of more than 30 selenoproteins, most of which have been discovered during the last decade. Se is incorporated, generally, as selenocysteine at the active center of a wide range of selenoproteins and functions as a redox center. The family of Se-dependent glutathione peroxidase (GSHPx) enzymes comprises the first characterized selenoproteins and represents the major class of functionally important selenoenzymes. Thioredoxin reductase reduces nucleotides in DNA synthesis and controls the intracellular redox state.[1] Se, thus, has structural and enzymic roles, the best known of which are the antioxidative function in the defense system of the cell and the catalytic role in the thyroid hormone metabolism.[1] Se has additional important health effects, which are not extensively linked to these enzyme functions. It is needed for the proper functioning of the immune system, it is the key component in counteracting the development of virulence and inhibiting HIV progression to AIDS, it is required for sperm motility, and may reduce the risk of miscarriages.[2] Now it is becoming increasingly clear that a relative deficiency of Se may be associated with an increased risk of developing cancer and cardiovascular diseases.[3,4]

Sources and bioavailability of selenium

Selenium enters the food chain through plants. Plant foods are the major dietary sources of Se in most of the countries. Se content of soil, which varies by region, determines the amount of Se in the plant foods that are grown in that soil, and the conditions affecting the bioavailability of the element is also important.[5] Se is hardly fixed in the soil and highly available for the plants where soil pH is high and precipitation and leaching is low, whereas high acidity, high level of sulfur and complexation with heavy metals, iron and aluminum decreases Se availability.[6] Animal-derived foods are rich in the element, however, bioavailability of Se in most plant-derived food is relatively higher.[7] Se exists in food in a number of organic and inorganic forms including selenomethionine (plant and animal source) and selenocysteine (mostly animal source and corn). Bioavailability and tissue distribution depend on the form ingested. Selenomethionine is more effective in increasing apparent Se status, because it is non-specifically incorporated into proteins in place of methionine. High levels of vitamin A, nutritionally adequate levels of methionin and/or total protein, antioxidants such as vitamin E, vitamin C can also enhance the bioavailability of dietary Se.[7] Despite the differences of bioavailability, meat, seafood, bread and cereals are considered the common sources of dietary Se in most part of the world. Therefore, the dietary Se intakes are likely to vary, mainly geographically, and this is reflected in differences in Se status of subjects living in different areas and different countries. However, in highly industrialized countries and large metropolitan cities, the human population does not depend solely on locally produced vegetable and animal products. Therefore, the effect of a Se-poor soil may not be reflected to the same degree in daily intake of the element and it can be significantly affected by differences in dietary habits.

Selenium in Turkey

There is a lack of detailed information regarding the soil content of Se in Turkey, although it has been reported that the concentration of Se in Turkish soil is

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somewhat lower than in other countries.[8,9] The data on Se content of foodstuffs produced in Turkey are also limited and confined with grain levels. Consumption of bread by an average socio-economical class individual is reported to be 400–450 g/day and this corresponds to almost half of the dry diet.[10] Therefore, it seems that most part of the dietary Se is dependent on the content of wheat, which is the main staple food in the country. Available data on the Se content of wheat, however, are not consistent and values reported vary widely by the area of production, and even by the year for the same area. ARAS and KUMPULAINEN[10] determined Se content of 1986, 1987, 1990, 1992, 1993 and 1994 Turkish wheat from four different regions and reported 32±6 μg/kg Se as a mean value. In a following study, conducted at the same institution with the same technique (INAA), on the 1995 and 1996 wheat products from the same three regions, highly different results were observed.[11] In two of the regions, average values were 84 (30–260) μg/kg, and 95 (65–130) μg/kg. In the third region, Se content was found to be highly enhanced compared to the previous years and a trend of continuous increase from the year 1986 (27 to 243 μg/kg) was noted. Our measurements using a spectrofluorometric method on the 1997 and 1998 wheat coming from almost the same areas showed a mean value of 81 (63–97) μg/kg, which were nearly in the same range as that of the latter study.[12] Corn samples collected from the local markets of Eastern Black Sea had an average Se content of 52 (29–81) μg/kg, which was lower than the average of Central Anatolia products (76 μg/kg).

Selenium status of Turkish population

The first data on Se status of Turkey was reported by our group as 88±12 μg/l serum Se for 76 children coming from middle to middle-upper income families living in Ankara.[13] We determined later the Se status of 218 subjects of a socio-economically heterogeneous group from the urban population of Ankara.[14] The mean Se levels were 45±10 μg/l in cord blood at birth, 74±14 μg/l in 2 to 16 years old children, and 74±16 μg/l in adults aged 18–48 years old. The study was extended later covering 274 subjects, aged 19–61 years, selected randomly from middle to middle-upper income families living in 7 different geographical parts of Turkey. Overall mean value of plasma Se was found to be 71±15 (28–114) μg/l. None of the regions were seemed to be deficient, and lowest mean values were observed in the Black Sea Region (Table 1).

Daily dietary intake of selenium

The only available data on the measured values of daily dietary intake of Se come from the studies of ARAS et al.[10,15,16] They have reported 81 μg/d for a group of ($n = 10$, METU) urban middle-upper-income individuals from Ankara, and 23 μg/d for a lower-income farmer group ($n = 6$, LAL) living in rural areas near Ankara.[16] They have then reported an average value of 52 μg/d for Ankara region.[10,15] Determinations on a university hospital diet with the same duplicate portion technique and INAA revealed values of 60 μg/d for summer diet ($n = 10$) and 38 μg/d for winter diet ($n = 8$). Thus, the overall average value of hospital diet was 49 μg/d.[10]

Table 1. Plasma concentration and estimated dietary daily intake of selenium in different regions of Turkey

Region	*n*	Plasma		Daily intake*		Daily intake**	
		Se, μg/l	Range	Se, μg/day	Range	Se, μg/day	Range
Central Anatolia	80	71 ± 11	51 – 96	45 ± 10	27 – 67	43 ± 11	25 – 65
Black Sea	100	66 ± 17	28 – 114	44 ± 14	17 – 84	39 ± 16	4 – 82
West	26	58 ± 15	28 – 85	33 ± 13	10 – 57	31 ± 13	4 – 55
Middle	25	58 ± 17	35 – 93	31 ± 12	17 – 60	31 ± 15	11 – 62
East	49	75 ± 15	42 – 114	49 ± 12	23 – 84	46 ± 17	17 – 82
Marmara	63	72 ± 10	54 – 96	–	–	–	–
Thrace	30	69 ± 9	55 – 88	–	–	–	–
Southern	33	75 ± 10	54 – 96	47 ± 9	26 – 64	46 ± 9	28 – 65
Mediterranean	31	78 ± 16	51 – 110	48 ± 15	21 – 80	49 ± 14	25 – 78
Overall	274	71 ± 15	28 – 114	44 ± 13	10 – 84	43 ± 13	4 – 82

Estimated as described by *LONGNECKER et al.,[17] and **HALDIMANN et al.[18]

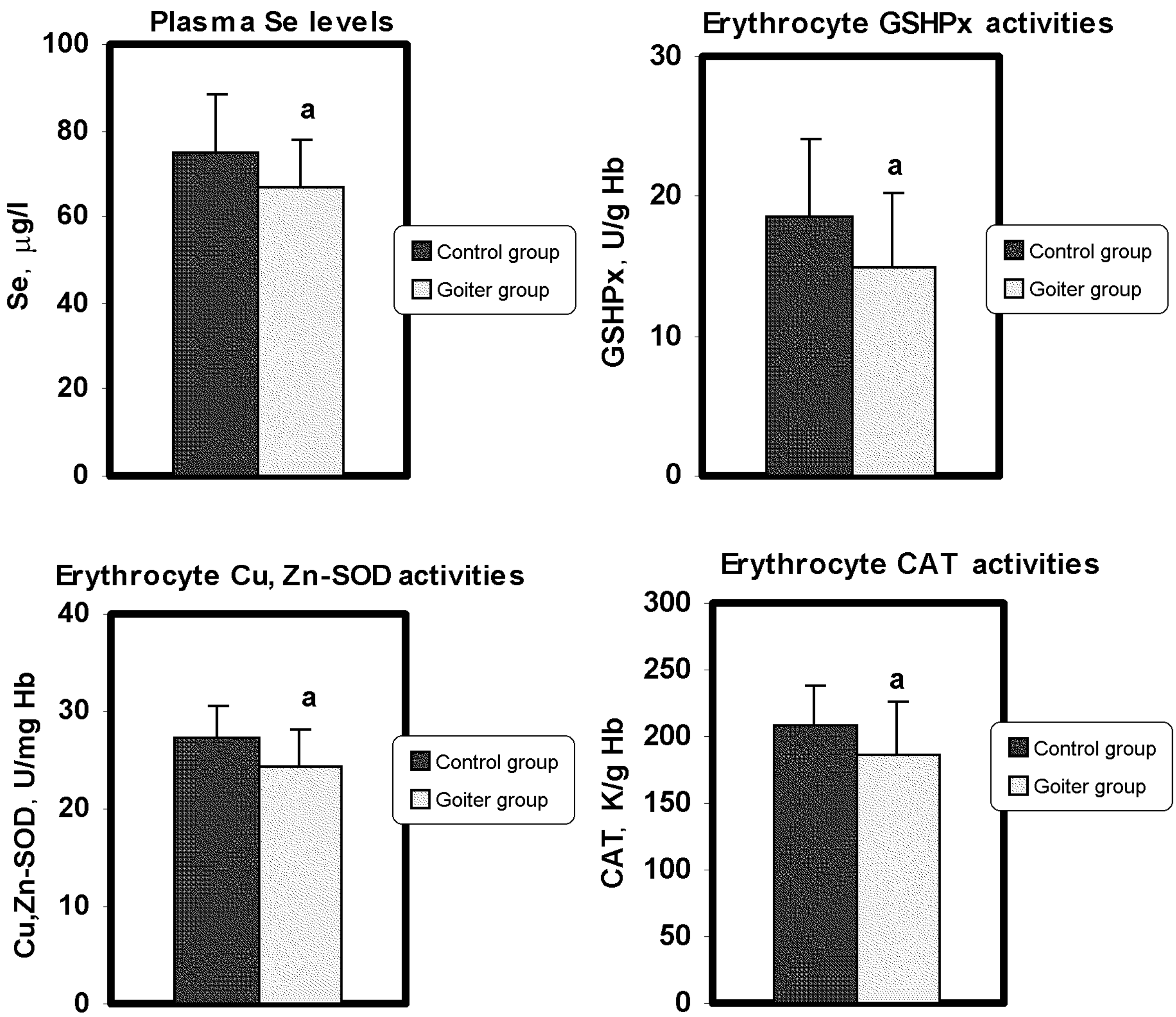

Fig. 1. Plasma Se levels and erythrocyte antioxidant enzyme activities in goiter and control children. Values are given as mean ±SD ([a] p<0.05)

Despite the fact that the double portion technique is the most precise method for evaluation of dietary daily intake, it is not easy and practical for applying to large number of samples, therefore, more convenient alternatives are needed. We have, thus, attempted to estimate the daily intake of Se by using an algorithm given by LONGNECKER at al.[17] and a regression curve calculated by HALDIMANN et al.[18] Both methods resulted in very similar values. The estimated value for Ankara region was 45 (or 43) μg/d, which was similar to that obtained by ARAS et al.[10,15,16] Therefore, it seemed to use this type of estimations which provided quite an accurate approximation and could be applied to unlimited number of samples. When both measured and estimated dietary intake values and relatively wide coverage of our data are considered, and compared with the recommended values (US RDA[19] and UK NRI,[4] which are 55 μg/d and 60–75 μg/d, respectively) it appears that the dietary intake of Se is low in Turkey.

Selenium and iodine

Thyroid hormones regulate and promote cellular growth and development, therefore, are essential for the maintenance of normal metabolic functions in living organisms. Iodine is a structural component and, thus, a primary requirement of the thyroid hormones. Se is also required for thyroid hormone synthesis, activation and metabolism due to its role in the antioxidant defense system, and due to the fact that iodothyronine deiodisases, which catalyze the deiodination of thyroid hormones are selenoproteins.[20] However, the relations between Se and thyroid function are complex and dual.

Table 2. Modified DNA base levels in goitrous and control children

	8-OH-Gua nmol/mg of DNA	8-OH-Ade nmol/mg of DNA	5-OH-Cyt, nmol/mg of DNA
Goiter (*n*=14)	0.05 ± 0.02	0.02 ± 0.007	0.03 ± 0.02
Control (*n*=14)	0.07 ± 0.02[a]	0.04 ± 0.01[b]	0.07 ± 0.03[b]

Values are given as mean ± SD.
1 nmol/mg of DNA corresponds to approximately 308 lesions/10^6 DNA bases.
[a] p<0.05, [b] p<0.01 by Student's *t*-test.

When Se deficiency accompanies to severe iodine deficiency, it may increase the damage in thyroid tissue where large amounts of H_2O_2 are generated as a cofactor to the synthesis of thyroid hormones. Se may also provide sparing of iodine by decreasing the catabolism of prohormone, thyroxin, T4, when a shortage of iodine intake exists.[21]

Both of these essential trace elements are inadequately available for human beings and livestock in great parts of the world. Existing data suggest that none of the regions of Turkey is free of endemic goiter. Therefore, we conducted a study in the Eastern Black Sea that is recognized to be one of the highest goiter prevalence rate regions of Turkey, with the aim to investigate the alterations of oxidant and antioxidant status and oxidative DNA base damage in iodine-deficient goitrous children and the possible link between them. After screening the whole population of high schools of two towns by neck palpation, a goitrous group and a control group were selected by a simple random sampling technique, and were ranked according to WHO criteria using urinary iodine (UI) levels. Thus, the goitrous group ($n = 45$) was composed of severely or moderately iodine deficient (UI<5 μg/dl) children aged 15–18 years. Control group ($n = 42$) consisted of non-goitrous and mildly iodine deficient or normal iodine status (UI>5 μg/dl) children with the same gender and age. Plasma Se and UI levels; erythrocyte GSHPx, superoxide dismutase (Cu, Zn-SOD) and catalase (CAT) activities were determined, as described earlier.[22,23]

The goiter prevalence in the region was found to be 39.6%. Erythrocyte GSHPx, Cu, Zn-SOD and CAT activities of goitrous group were significantly lower than the control group. Mean plasma Se levels was found to be 67±11 μg/l and 75±14 μg/l (p<0.05) for the goitrous and control groups, respectively (Fig. 1). The daily intake of selenium, estimated by the above-mentioned methods were lower than the RDA value of 55 μg/day in both goitrous (39 or 42 μg/day) and control (46 or 49 μg/day) groups. Modified DNA base levels were determined in both groups ($n = 14$) by gas chromatography/isotope dilution mass spectrometry with selected ion monitoring.[24] The levels of 8-OH-Gua, the commonly used biomarkers of oxidative DNA damage; 5-OH-Cyt, the more mutagenic than any other DNA lesions; 8-OH-Ade, a prominent purine lesion, possesses premutagenic properties, were found to be significantly higher in the goitrous group (Table 2). Whether the high level of oxidant stress encountered in goitrous populations is a cause or a consequence of the thyroid damage, need further investigations. However, our results, seem to suggest a link between antioxidant status, including Se, and DNA base damage and, hence, the development of benign and possibly malign thyroid diseases.

Conclusions

Measured and estimated values of dietary Se in Turkish population appear to be lower than the recommended values. However, as in the case of group LAL,[10,15,16] there could be some areas, particularly in the rural part of the country, where the dietary intake of Se may be more lower and even severely deficient due to the confinement of the diet to the limited products locally produced, poor quality and/or poor Se content of the soil, and the dietary habits. When the prevalence of iodine deficiency in the most parts of the country is considered, the importance of adequate intake of Se becomes more obvious. Therefore, more coordinated effort is needed to elaborate the exact Se profile of Turkey.

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