Studies on Human Selenium Requirements in China

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ABSTRUCT

The field intervention in China has been done to establish the fact that Keshan Disease is related to the poor selenium (Se) of the local soils and can be prevented by the supplementation of Se. However, there also have certain seleniferous areas in china where chronic selenosis in the local inhabitants still persisted. Since 1982, we have been carrying out the determination on human Se requirements in the areas with different Se levels. The minimum physiological requirement and the range of daily safety intake for adults were 50 and 50-250 μg/ day, respectively.

INTRODUCTION

Selenium has been shown to be essential trace element for humans[1,2)]. High incidence of Keshan Disease (KD), which is an endemic cardiomyopathy widely distributed in China, has been reported to relate poor selenium in the local soils[3)] and can be prevented by the supplementation of selenium[1)]. However, there also have some seleniferous areas in China. A heave prevalence of human selenosis in a certain seleniferous area of China occurred in 1961-1964[4)].

In recent years, the epidemiologic investigations have shown the association of cancer mortality and cardiovascular disease incidence with low selenium status[5,6)], which suggested that selenium status might be able to modify the risk of cancer and cardiovascular disease and thus has been received great attention. Since 1982, we have been carrying out the determinations on human selenium requirements in the areas with different selenium levels in order to develop further supplementation or fortification to be used in the poor selenium areas, to acquire more definitive human nutritional standards for establishing Recommended Dietary Allowance (RDA), to examine the effect of long-term excess selenium intake on

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the health of populations in seleniferous areas and to provide information about the dosage regime appropriate in cancer prevention trials. This paper reviewed the results obtained for adults based on investigation on the local residents in the low, normal and high selenium areas for selenium content in foods, and the minimum physiological requirement and the daily safety range of intake, respectively.

METHODS

Selenium content in foods. The food samples in Non-KD site were taken from the Shiba brigade, Huanglian Commune in Sichuan Province where is the so-called safety island surrounded by the latter KD area; the samples in KD site were taken from several production teams in Huangshui Commune where are KD area[7]. The samples in the normal, medium and high selenium sites were collected from the high selenium area or the sites adjacent to this area in Enshi County, Hubei Province, respectively.

Supplementary study on the minimum physiological requirement. This study was carried out at Institute of Nutrition and Food Hygiene in Beijing of china. Subjects were the staff of this Institute (18-44 years of age). All subjects dined at the laboratory during the whole experiment and food intake was recorded for calculating selenium intake. The subjects were randomly divided into two groups of four males and two females each. The supplemented doses for each group were weekly increased from 0, 300, 700 to 900 μg Se/ day as sodium selenite or DL-selenomethionine. Selenium concentration and glutathione peroxidase (GSHPx) activity in plasma were determined. All samples were stored at -30°C until analysis. The basal diet for the subjects provided average daily selenium intake of 45.5 μg/ day for both sexes.

Analysis methods. Selenium concentration in plasma was determined with fluorimetric method[8]. GSHPx activity in plasma was determined by the coupled enzyme method[9,10]

RESULTS

Selenium content in foods

Selenium contents in foods from the areas with different selenium levels are shown in Table 1. Selenium content in foods from a KD area was significantly lower than that from the area of high selenium level. The selenium content in foods from the safety island is significantly higher than that produced in the nearby KD site. Most vegetables contained negligible amounts of selenium, but animal foods such as fish, shrimp, kidney, liver, meat and eggs are good sources of dietary selenium in KD areas. The foods taken from the area of high selenium contained large amounts of selenium compared with the samples taken from the other place.

Table 1. Selenium content of popular foods consumed by the local inhabitants in sites with different selenium levels[a]

Item	KD	Non−KD[b]	Normal	Medium	High
Rice, polished	0.006	0.015	0.113	0.198	1.071
Wheat	0.003	0.015	0.068	0.308	—
Noodles, dried	—	—	0.108	0.423	0.845
Maize flour	—	—	0.035	0.226	1.483
Soybeans, dried	0.012	0.072	0.128	0.485	2.200
Hezha[c], fresh	—	—	0.009	0.064	0.344
Legume products, fresh	—	—	0.044	0.276	1.343
Vegetables					
Beans, fresh	<0.001	0.001	0.015	0.485	1.219
Leafy, fresh	<0.001	0.001	0.029	0.064	1.464
Fruity, fresh	<0.001	0.002	0.008	0.169	1.024
Roots & tubers, fresh	<0.001	0.002	0.014	0.059	0.731
Cucurbits, fresh	—	—	0.013	0.106	0.300
Pickled	—	—	0.109	0.130	0.676
Nuts, seeds & fruits, dried	0.008	0.017	0.292	3.085	6.786
Garlic, fresh	0.001	—	—	0.211	8.858
Fish, fresh	0.168	0.127	0.787	—	4.105
Whole egg, fresh	0.061[d]		0.389	1.487	2.771
Egg white	—		0.261	1.358	2.447
Egg yolk	—		0.685	1.712	3.299
Pork, fresh	0.030[d]		0.140	0.308	1.317
Lung	—		—	0.270	0.783
Heart	—		—	0.196	1.402
Liver	0.055[d]		—	0.318	0.900
Kindney	0.613[d]		—	1.198	2.471
Pork, smoked	—		0.189	0.430	2.442
Chicken, fresh	0.034[d]		0.260	0.249	—

[a]Expressed as μg Se/g fresh food. The results in KD and Non−KD sites were cited from the study of human requirement in China[7].
[b]Safety island surrounded by KD area.
[c]Local hot dish consisting of soybean and vegetables
[d]Purchased the samples from the local market near this KD site and Safety island

Minimum physiological requirement

The selenium concentrations in plasma of group supplemented with selenite reached a plateau at 300 μg Se/day, but the plateau had not been observed in the group supplemented with DL-selenomethionine and the selenium concentration in plasma of this group still increased with the supplementation of selenium. However, GSHPx activity of both groups had not changed from the beginning (the basal diet provides average dietary selenium intake of 45.4 μg/day for both sexes) to the end highest dose (total intake of 945.4 μg Se/day) of the experiment (Table 2).

Table 2. Influence of selenium supplementation as selenite(SeL) or selenomethionine(Se-meth) on selenium levels and GSHPx activity in plasma of male and female adults

Week	Se suplemented[a] (μg/ day)	Plasma Se (μg/ ml) SeL	Se-meth	Plasma GSHPx activity[b] SeL	Se-meth
1st	0	0.097±0.012	0.102±0.025	0.40±0.05	0.40±0.01
2nd	300	0.128±0.011	0.152±0.012	0.40±0.04	0.42±0.08
3rd	700	0.128±0.025	0.207±0.015	0.39±0.06	0.41±0.08
4th	900	0.132±0.017	0.297±0.063	0.41±0.03	0.42±0.07

Results are means±S.E.
[a]To a basal diet
[b]Expressed as n mole NADPH/ min/ ml.

DISCUSSION

Selenium content in foods-It was suggested that lack of available selenium in the soil of KD areas caused lower selenium content in plant foods (Table 1) and in turn resulted in the low blood and hair selenium concentrations of the local inhabitants. This would be the "soil factor" responsible to one of the reasons for the occurrence of KD[3]. The traditional diet of the Chinese peasant is basically vegetarian and includes mainly cereals, beans, and vegetables with only seasonal variations in the kind of each component. All of the foods were locally produced. The selenium intake mainly is from staple cereals[4,7]. Therefore, selenium content available in local soils is the dominant factor to the selenium status of local inhabitants.

The minimum physiological requirement-The Study on the relation between blood selenium concentrations and GSHPx activity in New Zealand indicated[11] that erythrocyte enzyme activity varied with selenium concentrations up to about 0.14 μg/ ml, after that the enzyme activity reached a plateau which was interpreted to mean that the selenium for the enzyme was met and this dietary selenium intake would represent a dietary requirement.

In our previous study on the minimum physiological requirement of adults in KD area[12], we found a plateauing of plasma GSHPx activity among groups supplemented with 30, 60, and 90 μg Se/day as DL-selenomethionine, and a coincidence of activity among these three groups was obtained after the seventh month. Based upon the above suggestion, if plateauing of enzyme activity either in erythrocyte or in plasma is with the same mean, the minimum physiological requirement for adults would be around 40 μg Se/day. However, only 10.9 μg Se/day was directly from the food, the other (73%) of selenium intake in this group was quantitatively supplemented. The SD (0.6) was different from the individual variation of selenium intake (40 μg) from natural food so that the individual variation observed was too small to represent the truly individual variation of total selenium intake. In the other word, the individual variation of selenium intake was artificially reduced. Recently, when Levander[13], based on our results on the study of human selenium requirement, calculated a dietary selenium recommendation for the standard North American, he needed the individual variation from mean selenium intake in detail. The total standard deviation was calculated by following different methods[14]. 1. Daily selenium intake directly from food was 10.9±0.6 μg and the other (30 μg) was supplemented orally. Estimated total selenium intake was 42 μg (from 40.9+2SD). 2. Hypothesized the same variation about the daily supplementary 30 μg Se (SD=2.3), the total selenium intake was calculated to be 46 μg (40.9+2SD). 3. Extrapolated from the physiological response. The safety range of selenium intake was extrapolated from the physiological response when the daily selenium intake was 40.9 μg. Although the GSHPx activity in plasma had already reached a plateau and its variation had not related to selenium intake, the selenium concentrations in plasma significantly correlated ($p<0.01$) to the selenium intake (Fig. 1). The average selenium concentration in plasma was calculated to be 0.069 μg/ml±0.005 (SD) when the total selenium intake was 40.9 μg/day, then the corresponding selenium intake value (50 μg) can be found from Fig. 1 when the plasma selenium concentration was 0.069 μg/ml +2SD (2 ×0.005). This figures are in agreement with the result of 52 μg Se/day calculated by Levander[13] as a safety factor of 1.3 that is suggested.

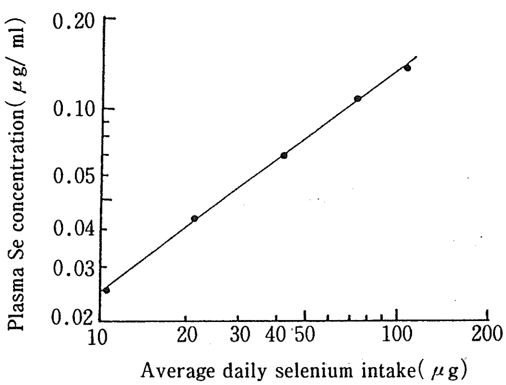

Fig. 1. Dose-Response Curve for average daily selenium intake and plasma selenium concentration($r=0.998$, $p<0.01$).

The results above were obtained in KD area. It has been reported that a posssible adaptation of populations to selenium levels in KD area would existed[15]. The results obtained in this study showed that the GSHPx activity for both groups of subjects from normal area had not changed from the basal diet to the highest dose (900 μg Se/day) which further confirmed that the minimum physiological requirement would be around 50 μg/day[14].

The range of daily safety intake-Based on the selenium content in foods and intakes in most countries, the safety range of selenium intake for the physiological requirement would be within 50-250 μg/day (Table 3).

Further investigation still continues as regards the maximum daily safety intake and marginal level of selenium poisoning.

Table 3. Evidence obtained for the estimation of safe level of selenium intake from selenium requirement study

Daily Se intake (μg)	Chemical form of Se ingested	Influence on human health
7	Natural vegetable diet	Keshan Disease occurred[7)]
17	Natural vegetable diet	Minimum requirement to protect from Keshan Disease[7)]
40.9	73% dietary Se as DL-selenomethionine	Physiological requirement to maintain plasma GSHPx activity at maximum[12)]
45.4	Natural diet	Physiological requirement to maintain plasma GSHPx activity at maximum
60	90% dietary Se as Na_2SeO_3	Plasma Se at maximum level[16)]
68.3	30% dietary Se as Na_2SeO_3	Plasma Se at maximum level
92	Natural diet	Dietary intake in Beijing[a]
90-168	Natural diet	Dietary intake in U.S., California[17)]
209	Natural diet	Dietary intake in U.S., eastern South Dakota[18)]
224	Natural diet	Dietary intake in Canada Halifax[19)]

[a]Unpublished

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