

Original

Deficient selenium status of a healthy adult Spanish population

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Abstract

Introduction: Selenium is an essential micronutrient for human health, being a cofactor for enzymes with antioxidant activity that protect the organism from oxidative damage. An inadequate intake of this mineral has been associated with the onset and progression of chronic diseases such as hypertension, diabetes, coronary diseases, asthma, and cancer. For this reason, knowledge of the plasma and erythrocyte selenium levels of a population makes a relevant contribution to assessment of its nutritional status.

Objective: The objective of the present study was to determine the nutritional status of selenium and risk of selenium-deficiency in a healthy adult population in Spain by examining food and nutrient intake and analyzing biochemical parameters related to selenium metabolism, including plasma and erythrocyte levels and selenium-dependent glutathione peroxidase (GPx) enzymatic activity.

Material and methods: We studied 84 healthy adults (31 males and 53 females) from the province of Granada, determining their plasma and erythrocyte selenium concentrations and the association of these levels with the enzymatic activity of glutathione peroxidase (GPx) and with life style factors. We also gathered data on their food and nutrient intake and the results of biochemical analyses. Correlations were studied among all of these variables.

Results: The mean plasma selenium concentration was $76.6 \pm 17.3 \mu\text{g/L}$ ($87.3 \pm 17.4 \mu\text{g/L}$ in males, $67.3 \pm 10.7 \mu\text{g/L}$ in females), whereas the mean erythrocyte selenium concentration was $104.6 \mu\text{g/L}$ ($107.9 \pm 26.1 \mu\text{g/L}$ in males and $101.7 \pm 21.7 \mu\text{g/L}$ in females). The nutritional status of selenium was defined by the plasma concentration required to reach maximum GPx activity, establishing $90 \mu\text{g/L}$ as reference value. According to this criterion, 50% of the men and 53% of the women were selenium deficient.

Conclusions: Selenium is subjected to multiple regulation mechanisms. Erythrocyte selenium is a good marker of longer-term selenium status, while plasma selenium appears to be a marker of short-term nutritional status. The present findings indicate a positive correlation between plasma selenium concentration and the practice of physical activity. Bioavailability studies are required to establish appropriate reference levels of this mineral for the Spanish population.

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Key words: *Selenium status. Glutathione peroxidase. Healthy adult population.*

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DEFICIENCIA DE SELENIO EN UNA POBLACIÓN ADULTA SANA ESPAÑOLA

Resumen

Introducción: El selenio es un micronutriente esencial para la salud del ser humano, debido fundamentalmente a su implicación como cofactor de enzimas con actividad antioxidante que protegen al organismo del daño oxidativo, de modo que una ingesta inadecuada de este mineral está asociada con la aparición y desarrollo de enfermedades crónicas tales como hipertensión, diabetes, enfermedades coronarias, asma y cáncer. Por esta razón, la determinación de selenio plasmático y eritrocitario contribuirá a la valoración del estado nutricional de la población estudiada.

Objetivo: El objetivo de estudio fue valorar el estado nutricional de selenio en una población adulta sana en riesgo de deficiencia, a través de una evaluación de la ingesta, así como de los niveles de selenio en plasma y eritrocito, y la actividad de la enzima selenio-dependiente Glutathione Peroxidasa (GPx) en eritrocito.

Material y métodos: El estudio se realizó en un grupo de población de 84 adultos sanos pertenecientes a la provincia de Granada (31 hombres y 53 mujeres) en los que se determinó la ingesta de nutrientes y selenio, sus niveles plasmáticos y eritrocitarios, así como su asociación con la actividad de la enzima Glutathione Peroxidasa y con diversos factores del estilo de vida.

Resultados: Las concentraciones medias de selenio en plasma fueron de $76,6 \pm 17,3 \mu\text{g/L}$ ($87,3 \pm 17,4 \mu\text{g/L}$ en los hombres, y de $67,3 \pm 10,7 \mu\text{g/L}$ para las mujeres), mientras que los valores eritrocitarios de selenio de la población total del estudio fue de $104,6 \mu\text{g/L}$ ($107,9 \pm 26,1 \mu\text{g/L}$ en hombres y $101,7 \pm 21,7 \mu\text{g/L}$ en mujeres). La evaluación del estado nutricional de selenio, se realizó en función de la concentración en plasma necesaria para alcanzar la máxima actividad de GPx, estableciendo como valor de referencia $90 \mu\text{g/L}$, observamos que el 50% de los hombres y el 53% de las mujeres se encuentran en situación de deficiencia.

Conclusiones: El selenio es un mineral sujeto a múltiples mecanismos de regulación. El selenio eritrocitario es un buen indicador del estatus mineral de selenio a largo plazo, mientras que el selenio plasmático es un indicador de estatus nutricional de selenio a corto plazo. Los resultados obtenidos mostraron una correlación positiva entre los niveles de selenio en plasma y la realización de actividad física. Es necesario disponer de más estudios de biodisponibilidad de selenio con el fin de poder establecer niveles de referencia de este mineral para la población española.

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Palabras clave: *Estatus de selenio. Glutathione peroxidasa. Población adulta sana.*

Introduction

The relationship between diet and numerous chronic diseases is well documented,^{1,2,3} and the eating habits of humans has become a major research field in developed countries.⁴ Assessment of the nutritional status of a specific group is a useful method for relating the habits of a population to their health status.⁵ Selenium deficiency alone is infrequent in developed countries, but an inadequate intake of this mineral has been associated with the development of cancer,⁶ asthma, and coronary disease, among other chronic conditions. Given the absence of symptoms, partial or subclinical deficiency is generally an incidental finding in biochemical analyses,^{7,8} either routine or ordered for another motive. Detection of this condition allows a rapid and total recovery of levels to be achieved through a balanced diet. The recommended selenium intake for healthy adults is considered to be 55 µg/day for females and 70 µg/day for males.⁹

An inadequate selenium nutritional status has been associated with Kashin-Beck disease^{10,11} and Keshan disease¹¹ which are endemic in some Chinese populations with a low intake of this mineral.⁴ These conditions are treated by supplementation with selenium. In developed countries, new trends in eating habits¹³ may produce micronutrient deficiencies that can manifest as growth restriction or other specific syndromes.¹⁴ Marked socio-cultural changes in Spain¹⁵ over recent decades have modified the diet of the population, with a possible impact on the intake of relevant nutritional components.¹⁶

With this background, the objective of the present study was to determine the nutritional status of selenium and risk of selenium-deficiency in a healthy adult population in Spain by examining food and nutrient intake and analyzing biochemical parameters related to selenium metabolism, including plasma and erythrocyte levels and selenium-dependent glutathione peroxidase (GPx) enzymatic activity.

Subjects and methodology

Subjects

The study population comprised 84 volunteers from Granada province (southern Spain), 31 males and 53 females aged from 21 to 59 yrs. Study exclusion criteria were: the presence of any disease that could affect their nutritional situation, the receipt of any nutritional supplement, and the withholding of informed consent to participation in the study, which was approved by the ethical committee of our institution.

Blood samples were drawn between 8 am and 10 am in fasting conditions. The individuals then underwent a personal interview for completion of a validated questionnaire on food consumption frequency, habits (smoking, drinking and physical exercise habits), and personal details¹⁷ and for gathering data on the clinical history.

Laboratory techniques

Blood samples were centrifuged for 15 min at 3,000 rpm to obtain plasma and erythrocyte samples (in 250-µl aliquots), which were stored at -80° C until their analysis. Samples were mineralized by wet method before the determination of serum and erythrocyte selenium levels. Selenium was measured by means of inductively coupled plasma mass spectrometry (ICP-MS), diluting plasma samples with Triton X-100 and nitric acid for the measurement of plasma selenium concentrations. GPx activity was determined by using the BIOXYTECH GPx-340™ kit, an indirect colorimetric assay (OxisResearch™).

Statistical analysis

Numerical data were expressed as arithmetic mean (± standard deviation [SD]) and standard error of the mean (SEM). Application of Kolmogorov-Smirnov test confirmed the normal distribution of the data. An analysis of variance (ANOVA) was performed. The parametric Student's t test was used for independent and related samples and the non-parametric Kruskal-Wallis test and Wilcoxon tests for independent samples and related samples, respectively. The Mann-Whitney test was used for intergroup comparisons of categorical data. Linear regression analysis was applied to determine bivariate correlations, using Pearson's correlation coefficient. Logistic regression analysis was performed to estimate the degree of association between each plasma variable and biochemical findings. $P < 0.05$ was considered significant in all tests.

Results

This sample of 84 healthy adults reported the following mean daily intakes: 1,946 ± 651 kcal of energy, 77.6 ± 34.7 g of protein, 91.01 ± 31.6 g of lipids, and 221.01 ± 81.9 g of carbohydrates. Figure 1 depicts these values as percentages of the total intake. Among food groups, cereals (55%), fruits (63%), or vegetables (56%) were consumed every day by 55-63% of participants.

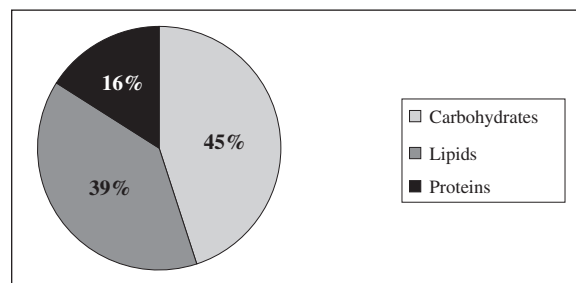


Fig. 1.—Percentage of macronutrients in diet of study population.

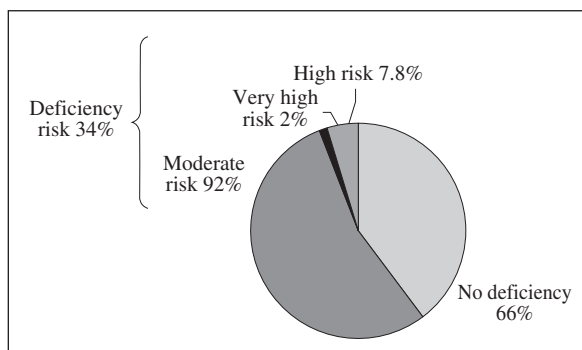


Fig. 2.—Percentage of subjects at risk of selenium deficiency.

The mean selenium intake of this population was $75.3 \pm 37.1 \mu\text{g/day}$ (range, 38.2-112.4 $\mu\text{g/day}$). It was below the recommended intake (RI) for healthy adults in 34% of the females ($< 55 \mu\text{g/day}$) and 34% of the males ($< 70 \mu\text{g/day}$). Stratification of these individuals at risk of selenium deficiency according to their intake showed (fig. 2) that 2% were at very high risk (intake $< 1/3$ IR), 7.8% were at high risk (intake $< 2/3$ IR), and 90.2% at moderate risk (intake between $2/3$ and IR).

The mean plasma selenium value was $76.6 \pm 17.3 \mu\text{g/L}$ (range, 45.6-121.0 $\mu\text{g/L}$): $67.3 \pm 10.7 \mu\text{g/L}$ in the females, and $87.3 \pm 17.4 \mu\text{g/L}$ in the males. When 90 $\mu\text{g/L}$ was considered as the minimum plasma concentration, 50% of males and 53% of females evidenced selenium deficiency; when 125 $\mu\text{g/L}$ was used as the reference value, 100% of males and 100% of females were selenium deficient.

Mean erythrocyte selenium values of the study population were $104.60 \pm 23.36 \mu\text{g/L}$ (69-160 $\mu\text{g/L}$): $120 \pm 21.48 \mu\text{g/L}$ in males and $101.7 \pm 21.67 \mu\text{g/L}$ in females. When 90 $\mu\text{g/L}$ was considered as the minimum erythrocyte selenium value, 30.4% of males and 37.7% of females were below this level.

A positive correlation was found between plasma and erythrocyte selenium levels (fig. 3) ($p = 0.009$; $r = 0.292$), and between erythrocyte GPx activity and

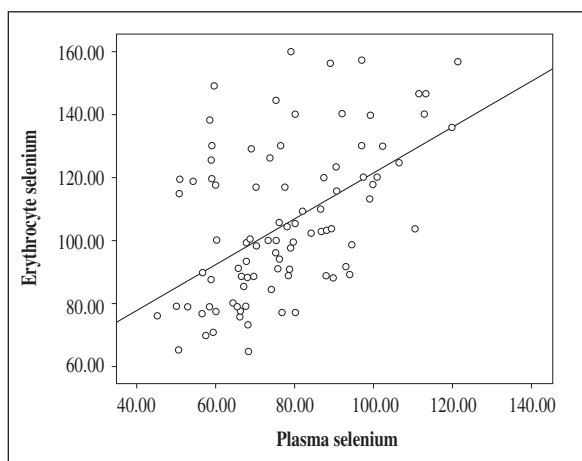


Fig. 3.—Relationship between erythrocyte and plasma selenium levels.

erythrocyte selenium concentrations ($p = 0.407$, $r = 0.001$).

The practice of physical activity was significantly and positively correlated with selenium intake ($p = 0.018$; $r = 0.266$) and with plasma selenium concentration ($p = 0.039$; $r = 0.227$). When the selenium intake was adjusted by the energy intake, a significant positive association was again found for the whole sample ($p = 0.009$; $r = 0.292$).

Discussion

The mean intake of selenium was below recommendations in one-third of the males and females in this population of healthy adults from Southern Spain. Plasma selenium levels were deficient in 60-100% of both males and females, depending on the minimum threshold value considered, and the erythrocyte selenium concentration was deficient in 30.4% of males and 37.7% of females, taking 90 $\mu\text{g/L}$ as minimum value. A significant and positive correlation was found between plasma selenium level and the practice of physical activity.

Interestingly, a deficient selenium intake was evidenced by 34% of both sexes, despite the distinct minimum recommendations for females and males (55 $\mu\text{g/day}$ vs. 70 $\mu\text{g/day}$). The mean plasma selenium concentration was low in our population ($76.6 \pm 17.3 \mu\text{g/L}$). The nutritional status of selenium is related to the plasma levels required to reach the maximum activity of GPx, which range between 90 $\mu\text{g/L}$ ¹⁸ and 125 $\mu\text{g/L}$ according to the literature.¹ Some authors have suggested that a healthy adult should have levels of around 100 $\mu\text{g/L}$.¹⁹ Reference plasma selenium values for each sex have not been published. In our sample, around half of the males and females could be considered selenium deficient when 90 $\mu\text{g/L}$ was taken as minimum threshold value, and all males and females could be considered deficient when 125 $\mu\text{g/L}$ was used as the reference level.

The mean erythrocyte selenium value of the study population (104.60 $\mu\text{g/L}$) was within the normal range (90-190 $\mu\text{g/L}$).²⁰ Nevertheless, taking 90 $\mu\text{g/L}$ as the minimum erythrocyte selenium value, 30.4% of males and 37.7% of females were found to be at risk of selenium deficiency.

The above findings are consistent with the daily consumption of cereals, fruit and vegetables reported by a large proportion of our sample, because these fiber-rich foods hinder selenium absorption and have shown a negative association with plasma selenium concentrations.^{21,22}

Most studies found no clear relationship between selenium levels and the practice of physical activity,^{1,21,23} suggesting that the increase in plasma selenium levels was due to the higher energy intake by individuals performing more physical activity. No other lifestyle factor studied (smoking, alcohol consumption, etc)

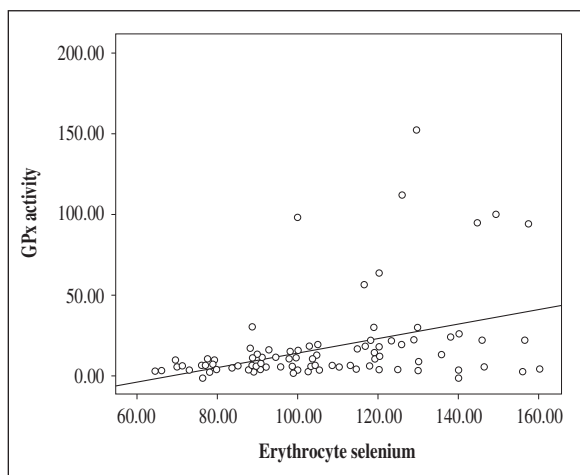


Fig. 4.—Correlation between GPx activity and erythrocyte selenium levels.

showed a significant association with plasma selenium levels. Accordingly, we analyzed the selenium intake adjusted by the energy intake, considering the study population as a whole, finding that the significant relationship with physical activity was maintained ($p = 0.009$; $r = 0.292$).

A significant and positive correlation was found between plasma and erythrocyte selenium levels. While plasma selenium is regarded as a good indicator of the short-term nutritional status of this mineral, erythrocyte selenium acts as a long-term marker due to the incorporation of selenium during cell synthesis; the red blood cells function, to a certain extent, as reservoirs of this mineral,⁴ which can then be released to meet the physiological needs of individuals.

A positive correlation was also observed between erythrocyte GPx activity and erythrocyte selenium concentration ($p = 0.407$, $r = 0.001$), confirming their dependent relationship (fig. 4). GPx appears to be the most sensitive indicator of selenium intake, showing higher activity at 1-2 weeks after the onset of supplementation, attributable to the short half-life (8-14 days) of platelets *versus* erythrocytes (120 days). However, GPx is part of a system of antioxidant reactions, and low GPx activity could be compensated by other components of this system, such as vitamin C and E. Nevertheless, the protective effect of GPx has a specific role when the organism is exposed to additional stress conditions; furthermore, individuals with vitamin E-deficient diets have a greater need for selenium.⁴ Selenium is highly involved in antioxidant defense as cofactor of numerous antioxidant enzymes.²⁴

Higher energy intake is generally associated with a greater consumption of protein and fat-rich foods, which may explain the increased plasma levels of TAG, total cholesterol, and LDL cholesterol and decreased HDL cholesterol levels with higher plasma and erythrocyte selenium levels. Other studies on healthy populations²¹ have shown a positive association between plasma selenium levels and the consump-

tion of meat and fish, which can both increase blood cholesterol levels. We found a positive correlation between plasma selenium level and uric acid, which may also be explained by meat consumption.

Conclusions

Selenium is subjected to multiple regulation mechanisms. Erythrocyte selenium is a good marker of longer-term selenium status, while plasma selenium appears to be a marker of short-term nutritional status. The present findings indicate a positive correlation between plasma selenium concentration and the practice of physical activity. Bioavailability studies are required to establish appropriate reference levels of this mineral for the Spanish population.

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