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Review

Revised reference values for selenium intake

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ABSTRACT

The German, Austrian and Swiss nutrition societies are the joint editors of the 'reference values for nutrient intake'. They have revised the reference values for the intake of selenium and published them in February 2015. The saturation of selenoprotein P (SePP) in plasma is used as a criterion for the derivation of reference values for selenium intake in adults. For persons from selenium-deficient regions (China) SePP saturation was achieved with a daily intake of 49 μg of selenium. When using the reference body weights the D-A-CH reference values are based upon, the resulting estimated value for selenium intake is 70 μg/day for men and 60 μg/day for women. The estimated value for selenium intake for children and adolescents is extrapolated using the estimated value for adults in relation to body weight. For infants aged 0 to under 4 months the estimated value of 10 μg/day was derived from the basis of selenium intake via breast milk. For infants aged 4 to under 12 months this estimated value was used and taking into account the differences regarding body weight an estimated value of 15 μg/day was derived. For lactating women compared to non-lactating women a higher reference value of 75 μg/day is indicated due to the release of selenium with breast milk. The additional selenium requirement for pregnant women is negligible, so that no increased reference value is indicated.

Contents

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1. Introduction

The D-A-CH 'reference values for nutrient intake' [1] are jointly issued by the nutrition societies of Germany, Austria and Switzerland [the abbreviation D-A-CH arises from the initial letters of the common country identification for the countries Germany (D), Austria (A) and Switzerland (CH)]. Currently, the 'reference values for nutrient intake' are being revised. Following vitamin D [2], calcium [3] and folate [4] the revised reference values for selenium were published in February 2015.

Selenium is an essential trace element present in a multitude of compounds. It is incorporated into proteins as selenocysteine. It is via these selenoproteins that selenium mainly has its effect. In the human genome, 25 genes for selenoproteins have been identified [5]. Among enzymatically active selenoproteins, selenocysteine is a central component of the active centre and directly involved in redox reactions. Glutathione peroxidases (GPx), thioredoxin reductases and deiodinases are among the group of well-characterised selenoproteins. The five human selenium containing GPx catalyse the reduction of hydroperoxides [6]. Selenoprotein P (SePP) is essential for the distribution and transportation of selenium, in particular to the brain and to the testicles [7].

2. Criteria for the assessment of selenium supply

The following parameters are used as biomarkers for selenium supply: the concentration of selenium in plasma or serum, the GPx activity in plasma (GPx3), in erythrocytes (GPx1), in thrombocytes (GPx1) or in whole blood (GPx3 and GPx1) and the concentration of SePP in plasma or serum. In principle the measurement of selenoproteins reflects the functional selenium pool bound to selenoproteins, whilst the total selenium content also includes selenomethionine that is unspecifically incorporated in proteins. Given maximum synthesis of selenoprotein, SePP and GPx3 together constitute a concentration of 80 μg to 90 μg of selenium/l of plasma [8].

Most reference values are based on the measurement of GPx activity in plasma. Meanwhile however, SePP concentration in plasma is deemed to be the most conclusive marker for determining the optimum supply of selenium [9–12]. The SePP concentration does not indicate a maximum level until a plasma selenium concentration of 100 μg/l to 120 μg/l is reached whilst GPx activity in plasma reaches its optimum at a lower level of approximately 90 μg/l [13,14]. In addition, nowadays there are improved analysis methods that allow determination of SePP. Based on human intervention studies, it is assumed that any further increase in the supply of selenium above and beyond a plasma selenium concentration of 120 μg/l will not lead to any further increase in selenoprotein expression [15]. However, in humans the data is limited to those selenoproteins ascertainable in blood, because tissue samples of bigger cohorts of healthy subjects are unavailable.

3. Derivation of the reference values for selenium intake

3.1. Adults

The basis for the derivation of reference values for selenium intake in adults is a study published in 2010, in which an adequate intake of selenium was established by means of the saturation of SePP in plasma [14]. In persons from selenium-deficient regions (China) with an average body weight of 58 kg SePP saturation was achieved with a daily intake of 49 μg of selenium [14]. This corresponds to a daily intake of approximately 1 μg of selenium per kg of body weight. Using the reference body weights the D-A-CH reference values are based upon (70.7 kg for men and 60.0 kg for women [1][1]), the resulting estimated values for selenium intake are 70 μg/day for men and 60 μg/day for women (see Table 1). Notably, these reference values are calculated for normal-weight adults.

Table 1
Estimated values for adequate selenium intake.

Age	Selenium [μg/day]	
	m	f
Infants		
0 to under 4 months	10	
4 to under 12 months	15	
Children and adolescents		
1 to under 4 years	15	
4 to under 7 years	20	
7 to under 10 years	30	
10 to under 13 years	45	
13 to under 15 years	60	
15 to under 19 years	70	60
Adults		
19 to under 25 years	70	60
25 to under 51 years	70	60
51 to under 65 years	70	60
65 years and older	70	60
Pregnant women		60
Lactating women		75

3.2. Children and adolescents

No data is available regarding the selenium requirement for children and adolescents. Therefore, the reference values for children and adolescents are based on the values compiled for adults and are calculated taking into account differences in body weight and including varying growth factors to take into account requirements for growth (see Table 2). Growth factors were calculated as the proportional increase in protein requirement for growth relative to the maintenance requirement according to WHO [17] at the different ages [1]. When using the age groups and reference body weights the D-A-CH reference values are based upon [1], the resulting estimated values for selenium intake are: for 1 to under 4 year-olds 15 μg/day, for 4 to under 7 year-olds 20 μg/day, for 7 to under 10 year-olds 30 μg/day, for 10 to under 13 year-olds 45 μg/day and for 13 to under 15 year-olds 60 μg/day. For 15 to under 19 year-old boys, the resulting estimated value for selenium intake is 70 μg/day and for girls of the same age, 60 μg/day (see Table 1).

3.3. Infants

The derivation of reference values for selenium intake in infants aged 0 to under 4 months is based on the selenium content of breast milk, which is considered to be the optimal diet for infants [19,20]. Deficiency diseases occurred in China where the selenium content of breast milk was below 0.3 μg/100 ml [21]. In Germany the selenium content of breast milk is approximately 1.5 μg/100 ml [22–24]. Selenium content levels measured in colostrum are twice as high as in mature breast milk [24,25]. Given an average breast milk intake of 750 ml/day [26] a selenium intake of approximately 11 μg/day results. The estimated value for adequate selenium intake for breast-fed infants aged 0 to under 4 months is indicated as 10 μg (see Table 1).

[1] The reference measurements for height correspond to the median of the height measurements from the German Health Interview and Examination Survey for Adults (DEGS1) [16]. Body weight was calculated using the height measurements based on an assumed BMI of 22 kg/m^2.

Table 2
Calculation of the estimated values for selenium intake for children and adolescents taking differences in average body weight and growth factors into account.

Age [years]	Gender	Reference body weight [kg][a] [1]	Growth factor[b] [1]	Selenium intake taking reference body weights into account [μg/day][c]	**Estimated value for selenium intake (rounded) [μg/day]**
1 to under 4	male	13.9	0.25	17.2	**15**
	female	13.2	0.25	16.5	
4 to under 7	male	20.2	0.06	21.2	**20**
	female	20.1	0.06	21.3	
7 to under 10	male	29.3	0.13	32.8	**30**
	female	28.7	0.13	32.5	
10 to under 13	male	41.0	0.13	45.9	**45**
	female	42.1	0.11	46.8	
13 to under 15	male	55.5	0.10	60.4	**60**
	female	54.0	0.07	57.7	
15 to under 19	male	69.2	0.07	73.2	**70**
	female	59.5	0.02	60.9	**60**

[a] The reference measurements each correspond to the 50th percentile of the anthropometrical measurements used in the German Health Interview and Examination Survey for Children and Adolescents in Germany (KiGGS; 2003–2006) [18]. In each case the values stated are for the mid-point of the respective age range.
[b] Growth factors were calculated as the proportional increase in protein requirement for growth relative to the maintenance requirement according to WHO [17] at the different ages [1].
[c] Calculated from: estimated $value_{adults}$ × (reference body $weight_{children/adolescents}$/reference body $weight_{adults}$) × (1 + growth factor).
Estimated $value_{adults}$: men 70 μg, women 60 μg (see Table 1). Reference body $weight_{adults}$: age group 25 to under 51 years: men 70.7 kg, women 60.0 kg [1].

Along with the introduction of solid foods the consumption of breast milk declines. Since no data is available from Germany with regard to selenium intake via solid foods, the estimated value for infants aged 0 to under 4 months is used to derive the reference value for infants over 4 months of age (see Table 3). Taking into account the differences regarding average body weight an estimated value of 15 μg/day for infants aged 4 to under 12 months was derived (see Tables 1 and 3).

3.4. Pregnancy

During pregnancy there is a slightly increased requirement for pregnant women to cover the selenium requirement of the fetus. On average this amounts to 2 μg/day [28–30]. Since the additional requirement however is negligible, an estimated value for selenium intake during pregnancy of 60 μg/day is indicated (see Table 1).

3.5. Lactation

The selenium requirement in women is increased during lactation due to the amount of selenium that is secreted with breast milk while feeding the infant. Approximately 11 μg of selenium/day is secreted with breast milk (cf. derivation for infants). Taking a bioavailability of 70% [12] into account, an additional 16 μg/day is required during lactation. The estimated value for selenium intake for lactating women amounts to 75 μg/day (see Table 1).

4. Ensuring a sufficient selenium supply

Ensuring a sufficient supply of selenium is possible via a balanced wholesome diet. Cruciferous vegetables (such as broccoli and white cabbage) and bulb vegetables (such as garlic and onions) as well as mushrooms, asparagus and legumes such as lentils all may have a high selenium content, depending on the quality of the agricultural soil on which they were grown. In particular, vegetable foods produced in Germany have a relatively low selenium content since the soil is low in selenium. In Germany, therefore, foods of animal origin such as meat and eggs as well as fish are a more reliable source of selenium. In vegetarian diets particular attention should be paid to include selenium-rich nuts (such as Brazil nuts) and mushrooms [31].

5. Preventive aspects

In the following, the current available data on selenium in association with some health-related aspects is briefly described by citing recent studies including systematic reviews and meta-analysis, but without performing an evidence judgment based on a systematic literature research. Dietary reference values are aimed for healthy individuals, thus requirements of patients are not being addressed.

In epidemiological studies it has been possible to observe an inverse association between serum selenium concentration and mortality risk [32,33]. In an evaluation of the NHANES study, this inverse association was found only to exist in subjects with serum selenium concentrations of up to 130 μg/l whereas for serum concentrations of selenium of over 150 μg/l a slight increase in mortality risk was observed [34].

It is being discussed whether selenium may reduce the risk of cancer, especially bowel, lung and prostate cancer. This is indicated by an intervention study with 1312 participants from the USA (NPC study) with a history of non-melanoma skin cancer (NMSC)

Table 3
Calculation of the estimated value for selenium intake for infants aged 4 to under 12 months.

Age [in months]	Gender	Reference body weight [kg][a] [1]	Selenium intake taking reference body weights into account [μg/day][b]	**Estimated value for selenium intake (rounded) [μg/day]**
4 to under 12	male	8.6	15.4	**15**
	female	7.9	15.5	

[a] The reference measurements correspond to the 50th percentile of the WHO child growth standards [27] for the age of 8 months.
[b] Calculated from: estimated $value_{0–4months}$ × (reference body $weight_{4–12months}$ /reference body $weight_{0–4months}$).
Estimated value 0–4 months: 10 μg (see Table 1). Reference body weight 0–4 months: male 5.6 kg; female 5.1 kg [1].

[35]. Even though the primary endpoint (recurrence of NMSC) was unaffected, a supplement of 200 μg of selenium-enriched yeast reduced total cancer mortality and total cancer incidence. The clearest effects were seen amongst those participants who had the lowest basal plasma selenium concentration at a level of <106 μg/l [36]. Another large-scale intervention study (SELECT) revealed that a supplement of 200 μg selenomethionine per day in men with a basal plasma selenium concentration of >120 μg/l had no cancer preventive effects [37]. This was observed for the primary endpoint prostate cancer but also for secondary endpoints like lung, colorectal, and overall primary cancer. Based on that, the study was already stopped after 5.5 years instead of running for 7 years. A Cochrane Review of prospective cohort studies and randomised controlled intervention studies described a significant inverse association between selenium supply and cancer risk for the prospective cohort studies [38]. The significant association could not be observed consistently when analysing the controlled intervention studies [38]. This is not surprising since this analysis failed to take into account the selenium supply of the participants at the beginning of the studies. In a cohort study published after the Cochrane Review an inverse association between selenium supply and the risk of bowel cancer was observed [39].

An inverse relationship between selenium supply and the risk of cardiovascular diseases has been assumed since the 1970s and is mostly based on observational studies. It has not been possible to consistently confirm the inverse relationship in intervention studies [15]. Current systematic reviews also demonstrate that there is no consistent correlation between selenium supplementation and the prevention of cardiovascular diseases [40,41].

There are conflicting results regarding the relationship between selenium supply and the risk of type 2 diabetes mellitus [15]. In the SELECT study supplementation with 200 μg of selenium/day had no significant effect on the risk [37]. In the aforementioned NPC intervention study with 1312 participants and comparable selenium supplementation [35] the risk was significantly increased by selenium supplementation amongst those participants who already had plasma selenium concentrations of >120 μg/l at the beginning of the study [42]. The risk of developing type 2 diabetes mellitus was not the primary outcome in either of the studies.

Furthermore, anti-inflammatory, antirheumatic and antiviral effects of selenium are under discussion [15]. In addition a positive association between selenium supply and bone density was observed in one cohort study [43]. Some clinical studies have demonstrated that selenium-deficient patients with autoimmune thyroid disease benefit from selenium supplementation, although the data are conflicting and many parameters must still be defined [44].

6. Conclusion

SePP concentration in plasma is deemed to be the most conclusive marker for determining the optimum supply of selenium. Taking reference body weights for adults living in Germany into account SePP saturation can be achieved with a daily selenium intake of 60 μg for women and 70 μg for men. European data [12] shows that Europeans and certainly many inhabitants of areas with similarly low soil selenium concentrations are sub-optimally supplied with selenium and therefore selenium intake should be increased. The integration of selenium-rich food items into a balanced wholesome diet constitutes a meaningful measure to avoid an insufficient supply and deficiency. Supplemental intake beyond the amounts needed for the full expression of selenoproteins is potentially increasing health risks and is therefore not recommended.

Conflict of interest

None declared.

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