Selenium status of lactating women is affected by the form of selenium consumed\(^1-^3\)

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ABSTRACT The impact of providing selenomethionine (2.7 \(\mu\)mol Se) or selenium-enriched yeast (2.9 \(\mu\)mol Se) on the selenium status of lactating and nonlactating women with customary intakes of \(\approx 1.3 \mu\)mol Se/d was studied. Plasma selenium declined in unsupplemented lactating women but not in nonlactating women. Selenomethionine increased plasma selenium in both lactating and nonlactating women whereas selenium-enriched yeast increased plasma selenium only in nonlactating women. Erythrocyte selenium concentration was not significantly modified by lactation. Plasma glutathione peroxidase (GPx) activity decreased with duration of lactation in unsupplemented women and selenomethionine or selenium-enriched yeast supplementation prevented the decline. Milk selenium declined markedly for 20 wk after parturition in unsupplemented women. Selenomethionine significantly increased milk selenium concentrations whereas selenium-enriched yeast prevented a decline. These results clearly show that the source of selenium provided to lactating women can significantly influence selected indexes of selenium status, including milk selenium concentration. \textit{Am J Clin Nutr} 1993;58:649–52.

KEY WORDS Selenium, women, lactation, human milk, glutathione peroxidase

Introduction

Great strides have been made in the knowledge of the physiological significance of selenium since its discovery as an essential nutrient \(1\). Reproducing females and their offspring of all species appear to be particularly vulnerable to inadequate selenium intake. Clinical signs and symptoms of selenium inadequacy likely reflect changes in one or more selenium-containing proteins. Although several selenoproteins in blood and tissues of mammalian species are recognized, the best characterized of these is glutathione peroxidase (GPx; EC1.11.19) \(2\). The involvement of this enzyme in the protection of cells from damage caused by products of oxidative reactions and the regulation of prostaglandin biosynthesis raise intriguing questions about its physiological importance \(1–3\).

Increased selenium needs during lactation have been documented in both production and laboratory animals \(4–6\). Lactating ewes are frequently supplemented with selenium to prevent muscular dystrophy in their offspring \(4\). Likewise, selenium supplements for lactating mares are often recommended to guard against nutritional muscular dystrophy in the suckling foal \(5\). There is evidence supporting the possible inadequacy of the National Research Council’s recommendation of 0.1 \(\mu\)g Se/g for rats during pregnancy and lactation, for maintenance of either maternal tissue selenium content or GPx activity \(6\). Diets containing 0.2 \(\mu\)g Se/g as selenite may be more appropriate for both pregnant and lactating rats \(6\). In 1989 the Food and Nutrition Board of the National Research Council recommended daily allowances for selenium of 55 \(\mu\)g \((0.700 \mu\)mol\) for nonpregnant, nonlactating women and an additional 20 \(\mu\)g to cover the amount of selenium typically secreted in milk \(7\). Estimates for both nonlactating and lactating women are made with the assumption that 80\% of selenium is absorbed.

The selenium content of human milk depends on the geographic location of lactating women \(8, 9\). This geographic variation likely reflects selenium abundance of the soil and therefore the vegetation grown and consumed in the region. Maternal plasma selenium has been reported to be directly related to human milk selenium concentration and maternal plasma GPx activity \(10\). However, little information exists on the impact of controlled maternal intake on milk selenium concentration and on the selenium status of breast-feeding infants. Levander et al \(11\) reported that the process of lactation depressed plasma selenium concentrations in women. It is unknown whether this depression reflects physiological changes during lactation or is a result of alterations in the maternal selenium stores.

The purpose of this investigation was to assess the ability of maternal supplementation with seleno-D,L-methionine (SeM) or selenium-enriched yeast (SeY) to influence the selenium status of lactating women and their milk.

Subjects and methods

Subject selection and characteristics

Thirty-one lactating women were studied at 4, 8, and 12 wk postpartum. An additional group of nonlactating, postpartum

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women \((n = 22)\) also was studied. All subjects resided in or near Champaign-Urbana, IL. Eligibility requirements included absence of medical history of diabetes, tuberculosis, or perinatal infection or conditions with proven adverse effects on the fetus; gestational age of 37–42 wk; birth weight within the 10th and 90th percentiles of the National Center for Health Statistics standard (12); and a 5-min Appgar score of \(\geq 8\). The use of human subjects was reviewed and approved annually by the Institutional Review Board of the University of Illinois.

Women enrolled in this study had a mean maternal age of 26.8 y (range 17–33 y). All lactating women were married whereas 12% of the nonlactating women were single. Lactating mothers had a mean educational level of 15.5 y and nonlactating women had an average of 12.8 y.

**Experimental design**

The fifty-three women were assigned to one of three dietary supplement treatments: no supplemental selenium, 200 \(\mu g\) Se as SeM, or 200 \(\mu g\) Se as SeY. Assignment to treatments was double blind. The control treatments consisted of 14 lactating women (L) and 9 nonlactating (NL) women. Eight L women (L + SeM) and seven postpartum, NL (NL + SeM) women were provided with selenium supplements (Solgar Co, Inc, Lynbrook, NY) designed to contain 2.53 \(\mu mol\) (200 \(\mu g\)) Se as SeM. Similarly, nine L women (L + SeY) and six postpartum, NL women (NL + SeY) were provided with selenium supplements (Solgar Co, Inc) designed to contain 2.53 \(\mu mol\) (200 \(\mu g\)) Se as SeY from 4 to 8 wk postpartum. Direct analysis in the authors’ laboratory indicated selenium contents of 2.67 and 2.93 \(\mu mol\) Se in each SeM and SeY supplement, respectively. Supplements were taken each morning from 4 to 8 wk postpartum. All subjects were instructed to consume no other supplement containing selenium during the entire study period.

**Methods**

Dietary evaluations were performed and specimens of blood and milk collected at clinical visits at 4, 8, and 12 wk after birth. Dietary records were used to estimate selenium intake of all women and were recorded 3 d prior or subsequent to each clinical visit. All women were individually instructed about correct procedures for recording food-intake data. Published selenium values for food were used to calculate mean maternal selenium intake (13). Samples of human milk were obtained from each breast-feeding mother at each clinical visit by complete breast expression with the aid of an electric breast pump (model SMB-BR; Eg nell, Inc, Cary, IL). In addition, milk specimens were collected at 20 wk postpartum. Milk was stored at \(-70^\circ C\) before analysis.

At each clinical visit fasting blood samples (5 mL) were collected by venipuncture into EDTA-treated syringes (Sarstedt, Nürnberg, Germany). Plasma and erythrocytes samples were separated by centrifugation at 10 000 \(\times\) g at 4 \(^\circ\)C for 10 min and stored at \(-70^\circ\)C before analysis.

Selenium concentrations of plasma, erythrocyte (RBC), and milk samples were determined in duplicate by using a gas chromatograph equipped with an electron capture detector (model 5890A; Hewlett Packard, Avondale, PA) (14). All assays included National Institute of Standards and Technology (NIST) bovine liver (1577a) and nonfat bovine milk powder (1349). Intrasample precision for selenium was within 5%. GPx activity was measured on plasma and RBC fractions by using a modification of the coupled assay described by Paglia and Valentine (15). For RBC samples, Drabkin’s reagent was omitted, because it has been shown to inhibit enzyme activity (16). Hydrogen peroxide (JT Baker Chemical Co, Phillipsburg, NJ) was used as substrate. No sample was thawed more than twice before analysis. An internal control of pooled human plasma was stored with other hematological samples and analyzed with each assay to ensure adequacy of storing methods and reliability of each assay, which proved acceptable.

Plasma GPx activity is expressed per gram protein. Plasma protein content was determined spectrophotometrically by using bichinonic acid (BCA) reagent as formulated by Pierce (Rockford, IL). Erythrocyte GPx activity is expressed per unit (g) hemoglobin. Hemoglobin concentration of RBC fractions was determined by the cyanmethemoglobin method (17) by using reagents prepared by Sigma Diagnostics (St Louis, MO).

**Statistical analysis**

Data from this randomized, double-blind study were evaluated by using two-way analysis of variance with main effects of treatment and sampling period, as well as the treatment-by-period interaction (18, 19). If the main effect of period and the interaction term were not significant \((P > 0.20)\), they were removed from the model. Assumptions of normality and equal variance were checked for each variable and corrected when necessary. For maternal plasma selenium concentration, analysis of covariance was used to test for significant effects of supplementation while presupplementation values were controlled for. Multiple comparisons were made by using Fisher’s protected least-significant-difference test, and a probability value of \(P \leq 0.05\) was taken to be statistically significant. To test for possible associations among maternal selenium intake and milk selenium concentration, Pearson’s correlation coefficients were calculated.

**Results**

Mean daily selenium intake of L women was estimated to be 1.27 \(\pm\) 0.11 \(\mu mol\) Se/d. Dietary selenium intakes of groups L + SeM and L + SeY were 1.25 \(\pm\) 0.10 and 1.59 \(\pm\) 0.10 \(\mu mol\), respectively \((L + SeY > L + SeM \approx L; P < 0.05)\). Thus, the total intakes of selenium of L + SeM and L + SeY women were \(= 3.8\) and 4.1 \(\mu mol\), respectively. Estimated mean maternal dietary selenium intake did not vary significantly during this study.

A weak but statistically significant correlation \((r = 0.33)\) was observed between maternal selenium intake and infant selenium intake \((P < 0.01)\) (20). Maternal selenium consumption and milk selenium concentration were also weakly but significantly correlated \((r = 0.39, P < 0.001)\).

Maternal plasma selenium concentration decreased 14% from 4 to 8 wk postpartum in the nonsupplemented L group, and remained relatively constant at 12 wk postpartum (Table 1). This decrease was not observed in any other group, whether L or NL. Supplementation with SeM significantly increased plasma selenium concentrations in both L and NL women during the supplementation period. However, only SeY significantly increased plasma selenium in NL women. Selenomethionine supplementation exerted long-term positive effects on the RBC selenium concentration of L but not NL women (Table 1). Except for the increase in L + SeM women, RBC selenium concentrations did not vary significantly with time or treatment.
Table 1
Plasma and erythrocyte (RBC) selenium in lactating (L) and nonlactating (NL) women receiving or not receiving supplemental selenomethionine (+SeM) or selenium-enriched yeast (+SeY) from 4 to 8 wk postpartum.

<table>
<thead>
<tr>
<th>Group</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma selenium (μmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>1.74 ± 0.10†</td>
<td>1.51 ± 0.10</td>
<td>1.43 ± 0.10</td>
</tr>
<tr>
<td>L + SeM</td>
<td>1.25 ± 0.13§</td>
<td>2.46 ± 0.13§</td>
<td>1.87 ± 0.14§</td>
</tr>
<tr>
<td>L + SeY</td>
<td>1.53 ± 0.13</td>
<td>1.80 ± 0.14</td>
<td>1.66 ± 0.14</td>
</tr>
<tr>
<td>NL</td>
<td>1.25 ± 0.14</td>
<td>1.49 ± 0.13</td>
<td>1.47 ± 0.14</td>
</tr>
<tr>
<td>NL + SeM</td>
<td>1.65 ± 0.13</td>
<td>2.28 ± 0.13§</td>
<td>1.60 ± 0.13</td>
</tr>
<tr>
<td>NL + SeY</td>
<td>1.36 ± 0.14</td>
<td>1.75 ± 0.13</td>
<td>1.66 ± 0.13</td>
</tr>
<tr>
<td>RBC selenium (μmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>2.61 ± 0.19</td>
<td>2.51 ± 0.20</td>
<td>2.52 ± 0.20</td>
</tr>
<tr>
<td>L + SeM</td>
<td>2.72 ± 0.24</td>
<td>3.15 ± 0.24§</td>
<td>3.98 ± 0.33§</td>
</tr>
<tr>
<td>NL</td>
<td>2.61 ± 0.24</td>
<td>2.62 ± 0.28</td>
<td>2.94 ± 0.27</td>
</tr>
<tr>
<td>NL + SeM</td>
<td>2.57 ± 0.30</td>
<td>2.27 ± 0.28</td>
<td>2.14 ± 0.28</td>
</tr>
<tr>
<td>NL + SeY</td>
<td>2.75 ± 0.28</td>
<td>3.09 ± 0.30</td>
<td>2.72 ± 0.34</td>
</tr>
</tbody>
</table>

* † ‡ § Significantly greater than weeks 8 and 12, P ≤ 0.05.
† ‡ § Significantly different from L at same time period, P ≤ 0.05.
† ‡ § Significantly greater than weeks 12 and 4, P ≤ 0.05.
† ‡ § Significantly greater than week 4, P ≤ 0.05.
† ‡ § Significantly greater than weeks 4 and 8, P ≤ 0.05.

Data indicate a longitudinal decrease in maternal plasma GPx activity from 4 to 12 wk postpartum in unsupplemented L women (Table 2). Supplementation with SeM or SeY from 4 to 8 wk postpartum did not significantly alter plasma GPx activity. Providing NL women with either selenium supplement was not accompanied by a significant change in plasma GPx activity. Maternal RBC GPx activities among L and NL groups were similar at all time points and did not respond to selenium supplementation.

Analysis of variance provided evidence of significant effects of both postpartum lactation time (P < 0.0001) and interaction of this time with supplementation treatment (P < 0.02) on milk selenium concentration (Fig. 1). At 8 wk milk selenium was significantly higher (P < 0.05) in women given SeM and SeY than in those provided no supplemental selenium. Milk selenium significantly declined with time in all treatments (P < 0.001). In nonsupplemented women, milk selenium concentration significantly declined from 4 to 20 wk postpartum (P < 0.001). Supplementation with SeM resulted in a significant increase in milk selenium concentration during the time of supplementation (P < 0.01). However, upon withdrawal of supplementation, milk selenium content decreased so that by 20 wk postpartum, mean milk selenium concentration of L + SeM women was similar to that of nonsupplemented women. Milk selenium concentration of L + SeY women also increased slightly but not significantly during the period of supplementation. During the remainder of this observational period, milk from L + SeY women continued to decline similar to that with other treatments.

Discussion

Plasma selenium concentrations are considered one of the most practical indicators of an individual’s selenium status (1, 2). These results clearly show that the form of selenium consumed can significantly influence plasma selenium in lactating women. SeM was more effective than was SeY in increasing plasma selenium concentration. In studies with Finnish lactating women SeY was more effective than inorganic forms of selenium in increasing blood selenium concentration (21). Levander et al (22) also observed that SeY was more effective than was selenite, and as effective as wheat selenium in increasing plasma and RBC selenium concentrations in middle-aged Finnish men. Collectively,
the present studies and those previously published by Kumpulainen et al (21) and Levander et al (22) suggest that inorganic forms of selenium would have a minimal impact on the selenium status of breast-feeding women. The apparent inability of SeY to increase plasma selenium in the present study compared with studies by Kumpulainen et al (21) may be explained by the fact that women in our study already had significant selenium stores, as reflected by ≈50% higher plasma selenium values, and received supplements for a shorter duration. Although SeY contains SeM there are other selenium compounds that remain to be identified (23). SeM appears to be one of the more effective forms of supplemental selenium that increases plasma selenium of lactating women. Nevertheless, plasma selenium concentrations were only weakly correlated with milk selenium concentrations.

These investigations clearly show that milk selenium decreases with the duration of lactation in women not receiving supplemental selenium. This observation is consistent with data of Kumpulainen et al (21) in women with apparently less adequate selenium stores than investigated in the present study. A decline with the progression of lactation has not been consistently observed in women residing in the United States (10, 11). The reason for this apparent inconsistency among studies is unknown, but may relate to maternal plasma selenium concentration and presumably the form and quantity of selenium consumed. From the present study and that of Kumpulainen et al (21), it is clear that the form of selenium supplemented is a decisive factor for determining the quantity of selenium in milk. Similarly, vegetarian and nonvegetarian women with similar intakes of selenium have been shown to produce milk with markedly different selenium concentrations (286 vs 208 nmol/L, or 22 vs 16 ng/mL, respectively) (8). Collectively, results of these studies indicate that form, and possibly bioavailability, of selenium consumed are important factors determining whether milk selenium declines with lactation.

Human milk selenium values in milk from women residing in countries with traditionally low selenium intakes, such as New Zealand, Finland, and Sweden, have been reported to be ≈130 nmol/L whereas values in the United States have been ≈225 nmol/L. The present studies demonstrate that during prolonged lactation milk selenium concentrations of lactating women in the United States decline to values comparable with those occurring in countries with lower selenium intakes. Thus, the value of supplemental selenium may be enhanced during prolonged lactation.

Overall, the results of this study show that dietary selenium intakes > 100 μg/d by lactating women can influence their plasma and milk contents of this trace element. Although these changes are reflected in the plasma and RBC selenium concentrations of their infants, as noted in the accompanying manuscript, they are not accompanied by similar increases in plasma GPx activity, a functional measure of selenium status (20).

We extend our sincere appreciation to the families who participated in this investigation; the entire staff of the pediatric and adolescent care unit at Christie Clinic, Champaign, IL; and Jennifer Andrews, whose superb technical assistance was an integral component of this project.

References