Bioavailability of Nutrients and Other Bioactive Components from Dietary Supplements

Effect of Reproduction on the Bioavailability of Calcium, Zinc and Selenium

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ABSTRACT Nutrient needs increase during pregnancy and lactation to support fetal growth and milk synthesis, respectively. Physiological adjustments that are made to meet those needs alter the fraction of ingested nutrient retained, or the bioavailability. Using stable isotopes as tracers, we measured calcium, zinc and selenium homeostasis in women during reproduction. The physiological response, and therefore the bioavailability, of these three minerals differed during reproduction. Calcium absorption increased ~2-fold during pregnancy but dropped to values for nonpregnant women during lactation. The calcium needs for lactation were met by renal conservation and bone resorption. In women chronically consuming a low calcium diet, fractional calcium absorption increased to >80% during reproduction. Zinc absorption tended to increase during pregnancy and lactation; renal conservation was not evident at any time during the reproductive cycle. Selenium absorption was high, ~80% of intake, in both pregnant and nonpregnant women. Pregnant women conserved selenium by decreasing urinary selenium excretion. Studies defining the impact of maternal status and the dietary mineral source and amount on mineral bioavailability are needed to determine the potential benefits of mineral supplementation during reproduction. J. Nutr. 131: 1355S–1358S, 2001.

KEY WORDS: • calcium • zinc • selenium • pregnancy • lactation • bioavailability

Bioavailability is defined as the proportion of the ingested nutrient that is used for normal physiological functions or storage (Jackson 1997). The proportion of the nutrient absorbed from the gastrointestinal tract is a major determinant of bioavailability, but that is not the only factor that influences bioavailability; tissue utilization of the absorbed nutrient or renal conservation can also be factors. Two types of minerals are discussed in this review: those regulated primarily by gastrointestinal absorption (calcium and zinc) and those regulated by renal conservation (selenium).

Bioavailability is influenced by endogenous and exogenous factors. Body status, or need, is a primary endogenous factor. Need increases during growth, pregnancy and lactation, and therefore the bioavailability of nutrients changes during those periods. Other endogenous factors include the previous intake of the nutrient, the efficiency of digestion, gut transit time and the presence of gastrointestinal disorders or disease (Jackson 1997). The purpose of this workshop was to evaluate the bioavailability of vitamin/mineral supplements. Exogenous factors likely to influence the bioavailability of supplements include whether they were consumed with food or water and, if they were consumed with food, the characteristics of the food eaten.

The bioavailability of supplemental iron during pregnancy and lactation has been studied and is reported in another article in this supplement. The bioavailability of other prenatal supplements has not been evaluated. This review therefore focuses on the physiological adjustments in nutrient utilization during reproduction in women. Using stable isotopes as tracers, we measured calcium, zinc and selenium homeostasis in women during reproduction. The results of those studies are reviewed here (Fung et al. 1997, Ritchie et al. 1998, Swanson et al. 1983).

Bioavailability of calcium and zinc during pregnancy and lactation

The total additional need for calcium during pregnancy and full lactation for 6 mo is estimated to be 65 g; the additional zinc need for the same period is estimated to be 370 mg. If there were no adjustments in calcium or zinc intake or in the net retention (i.e., bioavailability) of these two minerals, tissue reserves in the bone would have to be mobilized to meet the need for reproduction. This would cause a 7% decrease in bone calcium and an 80% decrease in bone zinc. If lactation were
continued for 2 y, as is usual in developing countries, 14% of the bone calcium and 140% of the bone zinc would be lost. Obviously, sufficient tissue reserves are not available to meet the entire reproductive need for calcium and zinc; other changes must occur.

In addition to tissue mobilization, changes in intake or nutrient bioavailability are two options for meeting calcium and zinc requirements for reproduction. A change in nutrient bioavailability may reflect an increase in true absorption, a reduction in endogenous gastrointestinal excretion or renal conservation. To ascertain the effects of reproduction on calcium and zinc bioavailability, we undertook a longitudinal study of 14 women. Exclusion criteria included low calcium intake (<800 mg/d), vegetarian diet, age of <22 or >42 y, self-reported body mass index (in kg/m²) of <17 or >27, daily intake of more than three cups of coffee or equivalent in caffeine-containing beverage, cigarette smoking, drug or alcohol abuse and chronic health problems (Fung et al. 1997, Ritchie et al. 1998). All of the women were white and were of upper to middle income stratum. The women were recruited before conception and studied at six time points: before pregnancy, 8–10 wk, 23–26 wk, 34–36 wk, early lactation, 7–9 wk and 5 mo after menses. The data from gestation and early lactation are reported here.

Using a weighed, 24-h food intake record, the women reported consuming 1054 ± 262 mg calcium/d and 10 ± 0.04 mg zinc/d before pregnancy. Because their intakes of calcium and zinc were good, they were told to maintain their dietary pattern throughout gestation. Changes occurred, however. The women increased their intake of dairy products, and consequently dietary calcium and zinc increased 28 and 32%, respectively, by the third trimester. Calcium and zinc intakes returned to near prepregnancy values during lactation.

The true, fractional absorption of calcium and zinc was estimated at each time point using stable isotopes of the two minerals and the dual isotopic tracer method (Eastell et al. 1989, Frigel et al. 1992). The women consumed 19 mg 44Ca and 3.0 mg 67Zn with a standard breakfast meal (an English muffin and peanut butter) at 0800 h after an overnight fast. Twenty-five minutes after the start of breakfast, 5.9 mg 44Ca and 0.8 mg 67Zn were infused into the antecubital vein. The stable isotopic ratios of calcium were measured in the first 24-h urine collection after isotope administration by thermal ionization mass spectrometry with a magnetic sector mass spectrometer (model 261; Finnigan MAT, San Jose, CA). The zinc isotopic ratios were measured in the first morning urinary voids on days 4, 5 and 6 after isotope administration and analyzed by induc-
tively coupled plasma mass spectrometry (model Sciex ELAN 500; Perkin Elmer, Norwalk, CT).

The true absorption of calcium increased significantly by 57 and 72% at the second and third trimester, respectively (P < 0.001), and it returned to near the prepregnancy level at early lactation (Ritchie et al. 1998). The true zinc absorption increased 29 and 33% at the second and third trimester, respectively, but this increase was not statistically significant. At early lactation, however, zinc absorption increased 73% and was significantly (P < 0.05) greater than that measured before conception. Based on an average intake of 1350 mg calcium in the third trimester, the women absorbed ~380 mg more calcium than during the prepregnancy period. The in-
crease in dietary zinc and true zinc absorption permitted the women to absorb an average of an additional 1.0 mg zinc/d in the third trimester and an additional 1.3 mg/d during lacta-
tion.

There was no evidence that either calcium or zinc was conserved by the kidney during pregnancy. Compared with before pregnancy, urinary calcium increased significantly by 46% and urinary zinc increased by 79% in the third trimester. The changes in urinary zinc were quite variable, however, and this large average increase did not reach significance. During lactation, the kidney reabsorption of calcium increased and the daily urinary output declined by 56% (P < 0.001) com-
pared with prepregnancy values. A similar decline in urinary zinc excretion did not occur; zinc excretion during lactation was similar to that in midpregnancy.

Approximately 99% of the whole body calcium and ~30% of the whole body zinc are found in bone. Although bone is not a true “store” of calcium and zinc, it appears that some of the mineral is a “functional reserve” that can be mobilized in time of need. The hormonal mechanisms for mobilizing cal-
caium and zinc are known; similar mechanisms for zinc have not been identified. Possibly, the release of zinc from bone is passive in conjunction with normal bone turnover rates.

We measured the changes in bone mineral density before conception, within 7 d of delivery and at early lactation using quantitative computed tomography (model DLO; General Electric, Milwaukee, WI). Pregnancy did not cause a significant change in trabecular bone mineral density of the lumbar spine. A 9% spinal trabecular bone loss was measured after only 2 mo of lactation, however. This bone loss during the early postpartum period is consistent with the findings of previous studies (Cross et al. 1995, Hayslip et al. 1989, Sowers et al. 1993). We estimate that this loss of bone in early lactation released daily 120 mg calcium and 0.9 mg zinc into the extracellular/plasma pool for uptake by the mam-
mary gland and use in milk synthesis.

In sum, the bioavailability, or fraction of ingested calcium and zinc that is retained, increases during pregnancy and lactation in response to an increased body need. The adjust-
ments for calcium differ from those for zinc during both preg-
nancy and lactation. In the study women, the additional need for calcium during pregnancy was met by an increased intake and a significant increase in gastrointestinal absorption. Zinc intakes also increased, but the rise in gastrointestinal absorp-
tion did not reach significance. There was no evidence of bone mineral mobilization or renal conservation. During early lac-
tation, trabecular bone was mobilized, releasing both calcium and zinc. Renal calcium conservation helped meet the calcium needs for lactation, whereas the high demand for zinc was met by an increase in fractional absorption. These diverse adjust-
ments in calcium and zinc during pregnancy and lactation suggest that their hormonal controls at these time points differ. However, the hormonal controls specific for pregnancy or lactation have not been identified for either mineral.

**Maternal calcium status and calcium bioavailability during reproduction**

The study of calcium homeostasis during reproduction was conducted in women who habitually consumed 1050–1350 mg calcium/d throughout the reproductive period (Ritchie et al. 1998). Most women around the world do not consume dairy products and have significantly lower calcium intakes. Studies in experimental animals show that the administration of a calcium-deficient diet during pregnancy or lactation exacerbates the adjustments in intestinal calcium absorption or bone demineralization (Garel 1987). Extrapolation from those studies to humans is not possible because of the shorter gestational periods in animals and the very severe deficiencies in dietary calcium that were studied. We therefore initiated a longitudi-
nal study of calcium metabolism in women living in Rio de Janeiro, Brazil, who habitually consume ~500 mg calcium/d
TABLE 1
Selenium absorption and balance in nonpregnant and pregnant women

<table>
<thead>
<tr>
<th></th>
<th>Nonpregnant women, n = 6</th>
<th>Early pregnant women, n = 6</th>
<th>Late pregnant women, n = 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se intake, µg/d</td>
<td>150 ± 2</td>
<td>154 ± 1</td>
<td>158 ± 2</td>
</tr>
<tr>
<td>Se absorption, %</td>
<td>78 ± 2</td>
<td>81 ± 1</td>
<td>84 ± 1</td>
</tr>
<tr>
<td>Tracer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balance</td>
<td>81 ± 0.4</td>
<td>78 ± 2</td>
<td>82 ± 1</td>
</tr>
<tr>
<td>Fecal Se, µg/d</td>
<td>28 ± 1</td>
<td>33 ± 1</td>
<td>28 ± 1</td>
</tr>
<tr>
<td>Urinary Se, µg/d</td>
<td>111 ± 2</td>
<td>100 ± 6</td>
<td>96 ± 2</td>
</tr>
<tr>
<td>Se balance, µg/d*</td>
<td>11 ± 2a</td>
<td>21 ± 4b</td>
<td>34 ± 2c</td>
</tr>
</tbody>
</table>

1 Data are means ± SEM. * P > 0.05. Values with different superscript letters indicate significant difference.
2 From Swanson et al., 1983.

(Vargas-Zapata et al. 2000). Nine women, aged 21–34 y, participated in the study. The women had an average parity of 2.6. All were healthy and nonsmokers and had no history of chronic disease. Supplemental iron was given during the second half of pregnancy, but none of the women received calcium supplements. Using the same methods as reported previously (Ritchie et al. 1998), dietary calcium intake, calcium absorption and urinary calcium excretion was measured at early pregnancy (10–12 wk), late pregnancy (34–36 wk) and early lactation (7–8 wk).

The women did not change their food intake during pregnancy or lactation. Calcium intake averaged 438 mg/d in early pregnancy, 514 mg/d in late pregnancy, and 451 mg/d in early lactation. At each time point, the true calcium absorption of the Brazilian women was roughly twice that of the U.S. women studied previously (Ritchie et al. 1998). In late pregnancy, true fractional calcium absorption averaged nearly 90%; absolute calcium absorption was ∼460 mg/d. True absorption in early lactation was similar to that at early pregnancy, i.e., ∼65%. This is the first study of intestinal calcium absorption in women consuming low calcium intakes during pregnancy. Calcium absorption was measured previously in lactating women from the Gambia who report intakes of ∼300 mg calcium/d (Fairweather-Tait et al. 1995). The Gambian women absorbed ∼1.6 times as much calcium as did women in the United Kingdom with intakes comparable to our U.S. women, ∼1200 mg/d.

It appears, therefore, that the bioavailability of calcium is enhanced in individuals with chronically low intakes and that when their need increases further due to gestation, the capacity to absorb calcium is even greater.

Selenium bioavailability during pregnancy and lactation

Knowledge about the absorption of selenium from foods or supplements does not predict its utilization, because bioavailability depends on the conversion of absorbed selenium into a biologically active form and tissue retention. There is no ideal method for measuring selenium bioavailability. Two approaches have been used: 1) the absorption, retention and/or tissue distribution of isotopically labeled selenium foods and 2) changes in the platelet glutathione peroxidase activity and/or plasma selenium concentrations. Selenomethionine is absorbed and retained more efficiently than inorganic selenite or selenite, and selenate is absorbed more efficiently than selenite, but it is not as effective at maintaining selenium status (as determined by platelet glutathione peroxidase activity) as is selenium-rich wheat or yeast (Fairweather-Tait 1997).

In a controlled metabolic study, we compared the selenium absorption, retention and excretion of pregnant women with that of nonpregnant controls (Swanson et al. 1983). A constant purified diet that provided the recommended intakes for all nutrients during pregnancy was consumed by all of the women. Selenium absorption was measured from egg whites and egg yolks intrinsically labeled with 76Se on d 8 of the 21-d study.

The selenium balance and absorption data are summarized in Table 1. Selenium absorption as estimated from the tracer and balance data did not differ. Group means for fractional absorption ranged from 78 to 84%. Selenium apparently is not homeostatically regulated by the gut. Renal regulation may be the means by which whole body selenium content is controlled. In this study, the pregnant women excreted less urinary selenium than did the nonpregnant women, and the conservation of selenium was more pronounced in late than in early pregnancy. The cumulative urinary excretion of 76Se supported that observation. Thus, pregnant women seem to meet their selenium needs for pregnancy by decreasing urinary losses.

It has been estimated that ∼5 kg of lean tissue is accumulated during pregnancy. If we assume that lean tissue contains 0.2–0.3 mg/kg selenium, the average daily retention over 280 d of pregnancy would be ∼3.5–5 µg. The net selenium retention in the second and fourth quarters of pregnancy was 10 and 23 µg/d, respectively (Swanson et al. 1983). Possibly, the high retention reflects the high intake of ∼150 µg/day during the 21-d metabolic study.

Future studies

Although most pregnant women in the United States are prescribed prenatal vitamin/mineral supplements, very little is known about the bioavailability of the nutrients in those supplements. In 1990, an Institute of Medicine report recommended that all pregnant women receive a multivitamin, mineral supplement (Table 2) (Institute of Medicine 1990). This formulation was based on nutrient need during gestation. Nevertheless, most pregnant women are prescribed prenatal supplements that contain all essential vitamins and minerals. This Institute of Medicine report also contained a number of research recommendations regarding nutrient supplements during pregnancy, which still must to be addressed. In particular, issues to be studied include the bioavailability of the chemical forms of nutrients commonly used in supplements.

TABLE 2
Recommended multivitamin mineral supplement for pregnancy women

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>30 mg</td>
</tr>
<tr>
<td>Zinc</td>
<td>15 mg</td>
</tr>
<tr>
<td>Copper</td>
<td>2 mg</td>
</tr>
<tr>
<td>Calcium</td>
<td>250 mg</td>
</tr>
<tr>
<td>Vitamin B-6</td>
<td>2 mg</td>
</tr>
<tr>
<td>Folate</td>
<td>300 µg</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>50 mg</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>5 µg</td>
</tr>
</tbody>
</table>

1 From the Institute of Medicine, Subcommittee on Dietary Intake and Nutrient Supplements during Pregnancy, 1990.
the interactions between nutrients in supplements, the effect of food on the bioavailability of prenatal supplements and the upper tolerance level of intake for nutrients during pregnancy and lactation.

LITERATURE CITED


