The Interaction between Calcium and Iron: Choice of Methodology Is Crucial for Outcome and Conclusions

Dear Editor:

The following comments relate to the interesting article by Gaitán et al. (1) in which they conclude that calcium does not inhibit the absorption of nonheme iron at single doses <800 mg Ca. This dose-response study reports on a very important topic, since, as also pointed out by the authors, both iron and calcium are essential nutrients. However, the study’s results are compromised by a methodological weakness that may affect the interpretation of the results.

In their study design Gaitán et al. (1) assessed iron absorption from single servings using radioisotope-labeled iron (5 mg) administered with increasing doses of calcium. Our comment is based on the fact that there is a well-known and considerable day-to-day variation in iron absorption within the same subject, which compromises assessment of iron absorption from single servings (2, 3). As a consequence, the majority of studies using iron radioisotopes in the evaluation of iron absorption assess the mean value following the administering of the study meal (or drink) on two consecutive days. Nevertheless, Gaitán et al. (1) assessed iron absorption from single servings. When administering the iron dose on two consecutive days and calculating the mean absorption from those days, the influence of the day-to-day variation in iron absorption is markedly reduced. Bjoñrn-Rasmussen et al. (3) observed that nonheme iron absorption from two identical meals (total iron content 3.0 mg/meal) served on two consecutive days and labeled with two different iron isotopes (55Fe and 59Fe) had a coefficient of variation (CV) of 36% between the two absorption measurements. Also Brise et al. (2) reported a CV of 35%, when using a similar design. The day-to-day variation stresses the importance of giving iron in repeated doses. Otherwise it is difficult to detect an actual difference in iron absorption from two different servings, as was the case in Gaitán et al. (1) where despite a mean difference of 30% in iron absorption when serving no calcium vs. serving 800 mg Ca, the difference was not significant (P = 0.09). The inability to statistically confirm such a clinically important difference displays a methodological weakness, which most likely can be attributed to the known day-to-day variation in iron absorption and the fact that only single servings were studied.

The choice of research method is crucial in determining the conclusions that can be drawn from the study. Thus, Gaitán et al. (1) should have considered the known variation in iron absorption. To draw accurate conclusions, in this case about dose-dependent inhibition of absorption, it is necessary to use the methods that have the necessary precision and accuracy.

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Literature Cited