Calcium and fracture risk

Jeri W Nieves and Robert Lindsay

A meta-analysis of cohort studies and clinical trials evaluating the effects of calcium on hip fractures by Bischoff-Ferrari et al (1) appears in this issue of the Journal. The authors’ analysis concluded that calcium, either in food or as a supplement, has no effect on hip fracture risk. This conclusion differs from that of the fracture prevention trials of calcium and vitamin D, as is at odds with the use of calcium (with or without vitamin D) as background therapy in clinical trials, and departs from the standard of care for osteoporosis prevention and treatment—where does that leave clinicians?

Osteoporosis is a complex disease whose pathogenesis often involves multiple factors. Even in controlled clinical trials involving calcium and vitamin D, the fracture effects have been relatively small, although often statistically significant. Perhaps these data suggest that calcium supplementation, to be effective, requires the addition of vitamin D supplementation. Recently, there has been a move to increase the recommendations for vitamin D intake. The realization that 25-hydroxyvitamin D concentrations <80 nmol/L are associated with markers of poor skeletal health (ie, increased parathyroid hormone concentrations, lower calcium absorption, and lower bone mineral density) has led several experts to recommend that vitamin D intake be increased to 1000 IU/d (from the current Dietary Reference Intake of 400 to 600 IU/d) with the goal of vitamin D–replete status, then a large segment of the population—where does that leave clinicians?

It is also possible that, in cohort studies such as those evaluated in this meta-analysis, there may be insufficient variability in calcium intake to allow detection of a fracture effect. In several of the cohort studies, mean baseline calcium intake was not reported; in those studies that noted mean calcium intakes, they were between 550 and 780 mg/d—an intake that is generally considered inadequate, although at least some persons will clearly be replete at even these intakes. Although Bischoff-Ferrari et al tried to address this problem (see Figure 3 in 1), without knowledge of the sample size per intake level, their analysis was limited. Furthermore, a single calcium assessment may not reflect usual calcium intake over the observation period of the study.

1 From the Departments of Medicine (RL) and Epidemiology (JWN), Columbia University, New York, NY, and the Clinical Research Center, Helen Hayes Hospital, West Haverstraw, NY (JWN and RL).

2 Reprints not available. Address correspondence to R Lindsay, Clinical Research Center, Helen Hayes Hospital, Route 9W, West Haverstraw, NY 10993. E-mail: lindsayr@helenhayeshosp.org.
As in any clinical trial, compliance and adherence also are issues of concern; compliance was noted to range from 42% to 77% in the few trials that evaluated these 2 factors. After compliance was taken into account, what was the actual intake in these populations? The adherence population analysis provided brought the pooled risk ratio for nonvertebral fracture in relation to calcium intake down to 0.83 (95% CI: 0.64, 1.09), which is similar to that seen in the combined calcium and vitamin D trials, although here it is clearly not statistically significant (3, 4).

A generalization from the literature, without a formal meta-analysis, may be that we need adequate supplies of both vitamin D and calcium to obtain significant reductions in nonvertebral fractures (especially hip fractures), and that those effects may be seen only in those persons who have insufficient vitamin D or calcium (or both). In addition, persons need to consume an overall healthful diet that meets all nutrient requirements. Protein for fracture prevention and healing (6–9) and plenty of fruit and vegetables for overall health (10, 11) are of particular importance. A well-rounded diet is important, and evaluation of one element or vitamin does not give the whole story.

So where does that leave clinicians? The best public health recommendation would be that people should consume an overall healthful diet including adequate consumption of both calcium and vitamin D. This meta-analysis highlights the importance of not segmenting nutrition into heterogeneous populations and isolated nutrients. Bone is not just calcium, and calcium does not function in isolation.

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REFERENCES


