Review: Calcium supplementation, with or without vitamin D, prevents osteoporotic fractures in people ≥ 50 years of age

Tang BM, Eslick GD, Nowson C, Smith C, Bensoussan A. **Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis.** Lancet. 2007;370:657-66.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Geriatrics ★★★★★☆☆ Rheumatology ★★★★★★☆

QUESTION

In patients ≥ 50 years of age, does calcium supplementation, with or without vitamin D, prevent osteoporotic fractures?

METHODS

Data sources: MEDLINE, EMBASE/Excerpta Medica, Current Contents, CINAHL, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews (all to January 2007); clinical trials repositories; resource Web sites; conference abstracts; review articles; and bibliographies of primary studies.

Study selection and assessment: Published or unpublished randomized controlled trials (RCTs) in any language that compared the effects of calcium, with or without vitamin D, with placebo on fractures or bone mineral density (BMD) in patients ≥ 50 years of age. Exclusion criteria were use of dietary calcium as an intervention, use of calcium as part of a nutritional supplementation regimen or combined with other treatment, secondary osteoporosis, and use of vitamin D without calcium. 29 studies met the selection criteria (n = 63 897, mean age 68 y, 92% women, median baseline risk for fracture 16%). Mean duration of treatment was 3.5 years. Dosage thresholds were set at 1200 mg/d for calcium and 800 IU/d for vitamin D. Quality assessment of individual studies was based on a 4-item checklist (reporting of randomization method, allocation concealment, blinding of outcome assessment, and completeness of follow-up).

Outcomes: Fracture of any site, including hip, vertebra, and wrist; only the first fracture in a given patient was counted as an event. Secondary outcome was percentage of change in BMD.

MAIN RESULTS

Meta-analysis showed that calcium, with or without vitamin D, reduced risk for fractures more than placebo (Table) and reduced bone loss in the hip (difference in mean BMD 0.54%, 95% CI 0.35 to 0.73; 24 trials, n = 44 990) and spine (difference in mean BMD 1.19%, CI 0.76 to 1.61; 24 trials, n = 3913).

CONCLUSION

Calcium supplementation, with or without vitamin D, prevents osteoporotic fractures and reduces bone loss at the hip and spine.

Source of funding: Australian Government.

For correspondence: Dr. B. Tang, University of Sydney, Penrith, New South Wales, Australia. E-mail benjamin@clubsalsa.com.au.

Calcium, with or without vitamin D, vs placebo for prevention of osteoporotic fractures*

Treatment	Number of trials (n)	Unweighted event rates	RRR (95% CI)	NNT (CI)
Calcium or calcium and vitamin D	17 (52 625)	12.12% vs 12.74%	12% (5 to 17)	63 (37 to 192)
Calcium only	9 (6517)	15.02% vs 16.72%	10% (0 to 20)	Not significant
Calcium and vitamin D	8 (46 108)	11.70% vs 12.19%	13% (3 to 23)	53 (29 to 500)

*Abbreviations defined in Glossary. Event rates and NNT (CI) provided by author. RRR and CI calculated from data in article

COMMENTARY

The meta-analysis by Tang and colleagues shows that, compared with placebo, calcium supplements ≥ 1200 mg/d can reduce fracture risk by up to 12% in men and women ≥ 50 years of age. Subgroup analyses showed that only those compliant with calcium had reduced fracture risk. This finding may explain why recent trials using intention-to-treat analyses failed to find an association between calcium and risk reduction (1). For clinicians, this finding highlights the importance of promoting lifelong adherence to calcium for bone health.

These results are not generalizable to persons obtaining calcium from dietary sources. Such persons could have even greater fracture reductions because of the micronutrients in dietary sources of calcium. Further, some evidence (2) shows that long-term adherence to calcium supplementation is better if changes are made to diet rather than by taking pills.

An important issue not addressed in this meta-analysis is the role of vitamin D in fracture prevention; Tang and colleagues found that adding vitamin D to calcium did not enhance treatment effect. This conclusion may seem surprising because there is a close relation between calcium and vitamin D in maintaining bone homeostasis, and with increasing age, calcium and vitamin D deficiency often coexist. Further, vitamin D deficiency is independently associated with decreased muscle strength, and some (3) but not all summary data (4) demonstrate that vitamin D, without calcium, can reduce falls. Thus, the physiologic rationale for using calcium and vitamin D for fracture prevention is persuasive. The lack of an effect of vitamin D in the meta-analysis by Tang and colleagues could be explained by the low doses of vitamin D in the included studies. Indeed, subgroup analyses found a greater treatment effect with increasing doses of vitamin D.

Until further studies are available, it seems reasonable for clinicians to prescribe vitamin D, in doses ≥ 800 IU, in addition to calcium.

Sophie A Jamal, MD, PhD
Helen Emanoilidis, MSc, RD
Multidisciplinary Osteoporosis Program, Women's College Hospital
Toronto, Ontario, Canada

References

1. **Jackson RD, LaCroix AZ, Gass M, et al.; Women's Health Initiative Investigators.** Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med. 2006;354:669-83.
2. **French MR, Moore K, Vernace-Inserra F, Hawker GA.** Factors that influence adherence to calcium recommendations. Can J Diet Pract Res. 2005;66:25-9.
3. **Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, et al.** Effect of vitamin D on falls: a meta-analysis. JAMA. 2004;291:1999-2006.
4. **Avenell A, Gillespie WJ, Gillespie LD, O'Connell DL.** Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis. Cochrane Database Syst Rev. 2005;(3): CD000227.