Review: Vitamin D supplementation decreases all-cause mortality in adults and older individuals

Autier P, Gandini S. **Vitamin D supplementation and total mortality: a meta-analysis of randomized controlled trials.** Arch Intern Med. 2007;167:1730-7.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Endocrinology ★★★★★☆☆

QUESTION

What is the effect of vitamin D supplementation on all-cause mortality?

METHODS

Data sources: PubMed, ISI Web of Science (Science Citation Index Expanded), EMBASE/Excerpta Medica, Cochrane Library, and bibliographies of selected studies, reviews, or books (to November 2006).

Study selection and assessment: Principal published reports of randomized controlled trials (RCTs) that assessed the effects of vitamin D supplementation (vitamin D_2 [ergocalciferol] or vitamin D_3 [cholecalciferol]), taken for any condition, on all-cause mortality. Trials had to randomize participants on an individual (rather than cluster) basis and include sufficient information to allow for calculation of relative risks and 95% CIs for all-cause mortality for vitamin D supplementation vs placebo or control. Trials that evaluated treatment with 1α-hydroxyvitamin D_3 (alfacalcidol), 1α,25-dihydroxyvitamin D_3 (calcitriol), or other vitamin D analogues in patients with advanced prostate cancer, chronic or end-stage renal disease, or those on renal dialysis were excluded. 17 RCTs and 1 quasi-RCT (n = 57 311, age range 33 to 106 y) met the inclusion criteria. Mean daily dose of vitamin D (adjusted for trial size) was 528 IU. Mean follow-up (adjusted for study size) was 5.7 years. Quality assessment of individual trials was not reported.

Outcomes: All-cause mortality.

MAIN RESULTS

4777 deaths occurred in the 18 trials. Meta-analysis of all trials showed that use of vitamin D supplements decreased the risk for all-cause mortality (Table). Meta-analysis of the 9 trials with sufficient power showed similar results (Table).

CONCLUSION

Vitamin D supplementation reduces all-cause mortality in adults and older individuals.

Source of funding: Not stated.

For correspondence: Dr. P. Autier, International Agency for Research on Cancer, Lyon, France. E-mail autierp@iacr.fr.

Vitamin D supplementation vs placebo or control for all-cause mortality*

Outcome at mean 5.7 y	Number of trials (*n*)	Event rates	RRR (95% CI)	NNT (CI)
All-cause mortality	18 (57 311)†	8.2% vs 8.5%	7% (1 to 13)	169 (91 to 1178)
	9 (55 774)‡	8.2% vs 8.5%	8% (1 to 14)	147 (84 to 1171)

*Abbreviations defined in Glossary. RRR, NNT, and CI calculated from data in article based on random-effects model.
†All trials.
‡All trials with acceptable power.

COMMENTARY

Vitamin D insufficiency, defined as biochemical evidence of deficiency without clinical signs or symptoms, corresponds to serum 25-hydroxyvitamin D levels of approximately < 20 to 30 ng/mL and is highly prevalent, affecting 25% to 70% of patients, depending on the subpopulation and season of year (1). Achieving adequate blood levels is clinically important because vitamin D affects more than bone health, and insufficiency has been associated with increased risks for some types of cancer, cardiovascular disease, hypertension, musculoskeletal pain, and type 2 diabetes.

The meta-analysis by Autier and Gandini pooled 18 trials of vitamin D supplementation among various study populations with baseline vitamin D levels consistent with insufficiency. The study participants were followed for a mean 5.7 years for all-cause mortality. Participants who received vitamin D supplementation had an 8% relative risk reduction and a small absolute risk reduction, which translates to approximately 1 death prevented for every 150 persons receiving supplementation. Because many persons are at risk, achieving adequate blood levels may have an important impact on both morbidity and mortality.

Current guidelines recommend 5 to 15 minutes of sun exposure at least twice weekly to the face, arms, hands, or back without sunscreen (2) and a daily vitamin D intake of 200 IU for persons ≤ 50 years, 400 IU for those 50 to 70 years, and 600 IU for those > 70 years (3). These recommendations may, however, be too conservative, and daily intakes ranging from 800 to 1000 IU or higher may be necessary to achieve 25-hydroxyvitamin D levels of 30 to 40 ng/mL. Because dietary sources rich in vitamin D are limited to fatty fish and some fortified foods, use of a vitamin D–containing supplement is a reasonable approach for patients who are at risk for, or have, vitamin D insufficiency.

Joel A. Simon, MD, MPH
San Francisco Veterans Affairs Medical Center
University of California, San Francisco
San Francisco, California, USA

References

1. **Hanley DA, Davison KS.** Vitamin D insufficiency in North America. J Nutr. 2005;135:332-7.
2. **Holick MF.** Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr. 2004;80:1678S-88S.
3. **Institute of Medicine, Food and Nutrition Board.** Dietary references intakes: calcium, phosphorus, magnesium, vitamin D and fluoride. Washington, DC: National Academy Press; 1999.