

Vitamin D Linked to Decrease in All-Cause Mortality

By Peggy Peck, Executive Editor, MedPage Today

Reviewed by Zalman S. Agus, MD; Emeritus Professor at the University of Pennsylvania School of Medicine.

September 10, 2007

LYON, France, Sept. 10 -- Vitamin D, widely touted for its ability to improve bone health, may also reduce all cause mortality by a small but statistically significant degree.

That finding emerged from a meta-analysis of 18 randomized trials which found that daily vitamin D in doses ranging from 300 to 2000 IUs reduced all cause mortality by 7% (95% CI 0.87-0.99). The analysis was published in the Sept. 10 issue of *Archives of Internal Medicine*.

The benefit was slightly greater -- an 8% reduction in all cause mortality -- when vitamin D was taken daily for three years or longer, wrote Philippe Autier, M.D., of International Agency for Research on Cancer here, and co-author Sara Gandini, Ph.D., of the European Institute of Oncology in Milano, Italy.

The mechanisms by which vitamin D would decrease mortality are not clear, but the authors suggested a number of possible explanations. These included the possibility that some effects of activation of the vitamin D receptor "such as inhibition of cellular proliferation and activation of cellular differentiation, could reduce aggressiveness of cancerous processes and expansion of atheromatous lesions."

The investigators analyzed data from 57,311 participants in 12 placebo-controlled trials and six open-label trials. The numbers of participants varied from 55 to 36,282 and the mean follow-up was 5.7 years, after adjusting for trial sizes.

Although there was a wide range in the daily dose of vitamin D, most were 400 IU to 833 IU, for a mean daily dose of 528 IU.

Among the findings:

Compared with baseline there was a significant increase in mean serum 25-hydroxyvitamin D₃ levels for all participants in active treatment groups versus a decline in mean serum 25-hydroxyvitamin D₃ levels among controls, but the increase was not related to vitamin D dose.

Compliance with vitamin D ranged from 48% to 95% across the 18 trials.

There were 4,777 deaths for any cause among the 57,311 participants.

In 13 trials active treatment included vitamin D and calcium supplementation, but the authors said the

mortality benefit was not likely to be the result of calcium supplements, because the five trials that did not include calcium supplements in the intervention group had a similar summary relative risk to those that included calcium.

Vitamin D is known to reduce fall and fracture risk among frail elderly patients by increasing postural stability, but 15 frail elderly patients need to be treated with vitamin D to prevent one fall. "Such an effect cannot translate into a 7% decrease in total mortality," they wrote.

In an accompanying editorial Edward Giovannucci, M.D., Sc.D., of the Harvard School of Public Health, wrote that given "the high probability of benefit for at least some of the many conditions that have been associated with vitamin D deficiency, and the low likelihood of harm, it seems prudent that physicians measure mean serum 25-hydroxyvitamin D₃ levels in their patients."

But while "a more proactive attitude to identify, prevent, and treat vitamin D deficiency should be part of standard medical care," Dr. Giovannucci concluded that the "roles of moderate sun exposure, food fortification with vitamin D, and higher dose vitamin D supplements for adults" are not yet clear and warrant further research and debate.

"Population-based, placebo-controlled randomized trials in people 50 years or older for at least six years with total mortality as the main end point should be organized to confirm these findings," Drs. Autier and Gandini concluded.

Action Points

Explain to interested patients that because the findings in this report are derived from a meta-analysis they need to be confirmed in a randomized, controlled trial.

Explain to interested patients that vitamin D has a number of confirmed benefits and is generally well tolerated.

Note that this study found no evidence that increasing the dose of vitamin D would increase the benefit.

Drs. Autier, Gandini, and Giovannucci reported no financial disclosures. No funding source was reported.