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Vitamin D supplementation for prevention of mortality in adults.

Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, Bjelakovic M, Gluud C.

Department of Internal Medicine - Gastroenterology and Hepatology, Medical Faculty, University of Nis, Zorana Djindjica 81, Nis, Serbia, 18000.

Abstract

BACKGROUND: The available evidence on vitamin D and mortality is inconclusive.

OBJECTIVES: To assess the beneficial and harmful effects of vitamin D for prevention of mortality in adults.

SEARCH STRATEGY: We searched The Cochrane Library, MEDLINE, EMBASE, LILACS, the Science Citation Index Expanded, and Conference Proceedings Citation Index-Science (to January 2011). We scanned bibliographies of relevant publications and asked experts and pharmaceutical companies for additional trials.

SELECTION CRITERIA: We included randomised trials that compared vitamin D at any dose, duration, and route of administration versus placebo or no intervention. Vitamin D could have been administered as supplemental vitamin D (vitamin D(3) (cholecalciferol) or vitamin D(2) (ergocalciferol)) or an active form of vitamin D (1α-hydroxyvitamin D (alfacalcidol) or 1,25-dihydroxyvitamin D (calcitriol)).

DATA COLLECTION AND ANALYSIS: Six authors extracted data independently. Random-effects and fixed-effect model meta-analyses were conducted. For dichotomous outcomes, we calculated the risk ratios (RR). To account for trials with zero events, meta-analyses of dichotomous data were repeated using risk differences (RD) and empirical continuity corrections. Risk of bias was considered in order to minimise risk of systematic errors. Trial sequential analyses were conducted to minimise the risk of random errors.

MAIN RESULTS: Fifty randomised trials with 94,148 participants provided data for the mortality analyses. Most trials included elderly women (older than 70 years). Vitamin D was administered for a median of two years. More than one half of the trials had a low risk of bias. Overall, vitamin D decreased mortality (RR 0.97, 95% confidence interval (CI) 0.94 to 1.00, I(2) = 0%). When the different forms of vitamin D were assessed separately, only vitamin D(3) decreased mortality significantly (RR 0.94, 95% CI 0.91 to 0.98, I(2) = 0%; 74,789 participants, 32 trials) whereas vitamin D(2), alfacalcidol, or calcitriol did not. Trial sequential analysis supported our finding regarding vitamin D(3), corresponding to 161 individuals treated to prevent one additional death. Vitamin D(3) combined with calcium increased the risk of nephrolithiasis (RR 1.17, 95% CI 1.02 to 1.34, I(2) = 0%). Alfacalcidol and calcitriol increased the risk of hypercalcaemia (RR 3.18, 95% CI 1.17 to 8.68, I(2) = 17%). Data on health-related quality of life and health economics were inconclusive.

AUTHORS' CONCLUSIONS: Vitamin D in the form of vitamin D(3) seems to decrease mortality in predominantly elderly women who are mainly in institutions and dependent care. Vitamin D(2), alfacalcidol, and calcitriol had no statistically significant effect on mortality. Vitamin D(3) combined with calcium significantly increased nephrolithiasis. Both alfacalcidol and calcitriol significantly increased hypercalcaemia.

Comment in

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