Annals of Internal Medicine | ORIGINAL RESEARCH

Oral High-Dose Multivitamins and Minerals After Myocardial Infarction

A Randomized Trial

Gervasio A. Lamas, MD; Robin Boineau, MD, MA; Christine Goertz, DC, PhD; Daniel B. Mark, MD, MPH; Yves Rosenberg, MD; Mario Stylianou, PhD; Theodore Rozema, MD; Richard L. Nahin, PhD, MPH; Lauren Lindblad, MS; Eldrin F. Lewis, MD; Jeanne Drisko, MD; and Kerry L. Lee, PhD, for the TACT (Trial to Assess Chelation Therapy) Investigators*

Background: Whether high-dose multivitamins are effective for secondary prevention of atherosclerotic disease is unknown.

Objective: To assess whether oral multivitamins reduce cardiovascular events and are safe.

Design: Double-blind, placebo-controlled, 2 × 2 factorial, multicenter, randomized trial. (ClinicalTrials.gov: NCT00044213)

Setting: 134 U.S. and Canadian academic and clinical sites.

Patients: 1708 patients aged 50 years or older who had myocardial infarction (MI) at least 6 weeks earlier and had serum creatinine levels of 176.8 μmol/L (2.0 mg/dL) or less.

Intervention: Patients were randomly assigned to an oral, 28-component, high-dose multivitamin and multimineral mixture or placebo.

Measurements: The primary end point was time to total death, recurrent MI, stroke, coronary revascularization, or hospitalization for angina.

Results: The median age was 65 years, and 18% of patients were women. The qualifying MI occurred a median of 4.6 years (interquartile range [IQR], 1.6 to 9.2 years) before enrollment. Median follow-up was 55 months (IQR, 26 to 60 months). Patients received vitamins for a median of 31 months (IQR, 13 to 59 months) in the vitamin group and 35 months (IQR, 13 to 60 months) in the placebo group ($P = 0.65$). Totals of 645 (76%) and 646 (76%) patients in the vitamin and placebo groups, respectively, completed at least 1 year of oral therapy ($P = 0.98$), and 400 (47%) and 426 (50%) patients, respectively, completed at least 3 years ($P = 0.23$). Totals of 394 (46%) and 390 (46%) patients in the vitamin and placebo groups, respectively, discontinued the vitamin regimen ($P = 0.67$), and 17% of patients withdrew from the study. The primary end point occurred in 230 (27%) patients in the vitamin group and 253 (30%) in the placebo group (hazard ratio, 0.89 [95% CI, 0.75 to 1.07]; $P = 0.21$). No evidence suggested harm from vitamin therapy in any category of adverse events.

Limitation: There was considerable nonadherence and withdrawal, limiting the ability to draw firm conclusions (particularly about safety).

Conclusion: High-dose oral multivitamins and multiminerals did not statistically significantly reduce cardiovascular events in patients after MI who received standard medications. However, this conclusion is tempered by the nonadherence rate.

Primary Funding Source: National Institutes of Health.

Ann Intern Med. 2013;159:797-804. www.annals.org

For author affiliations, see end of text.

* TACT Investigators are listed in the **Appendix**, available at www.annals.org.

Patients who maintain a diet rich in a highly complex mix of antioxidants and other micronutrients have lower rates of atherosclerosis (1–3). Clinical trials testing isolated and combination oral micronutrients have not replicated these benefits. Recent meta-analyses noted that only vitamins A, C, and E and the antioxidant mineral selenium have been tested in well-designed trials, with mixed results: High doses of vitamins A and E might increase risk for cancer in selected patients, vitamin C was inactive, and selenium might be beneficial (4, 5). Yet, studies of a few vitamins and minerals do not fully reflect the supplement use of a large segment of the U.S. population, which increasingly favors multivitamin and multimineral supplements.

TACT (Trial to Assess Chelation Therapy), a 2 × 2 factorial trial funded by the National Heart, Lung, and Blood Institute and the National Center for Complementary and Alternative Medicine (6, 7), assessed whether an EDTA-based chelation regimen or an oral high-dose multivitamin and multimineral supplement improved cardiovascular outcomes and was effective for secondary prevention in patients with a history of cardiovascular disease. The chelation results have been published (8). This article compares oral multivitamins and multiminerals with placebo.

METHODS

Design

This double-blind, 2 × 2 factorial trial randomly assigned patients to receive oral vitamins and intravenous chelation infusions, oral placebo and intravenous chelation infusions, oral vitamins and placebo intravenous infusions, and oral placebo and placebo intravenous infusions. The design and organizational aspects of TACT have been published (7). The institutional review board at each clinical site approved the study, and patients provided written informed consent. A data and safety monitoring board monitored the study.

See also:

Print

Related articles 806, 824
Editorial comment. 850
Summary for Patients. I-20

Web-Only

Supplement

