Hayam K. Shaker, MD
Hendersonville Family Practice Residency Program, Mountain Area Health Education Center, Hendersonville, NC

Sue Stigleman, MLS
Mountain Area Health Education Center Family Medicine Residency Program, Asheville, NC

ASSISTANT EDITOR
Anne L. Mounsey, MD
University of North Carolina, Chapel Hill

Q/ Can calcium supplements cause serious adverse effects in healthy people?

EVIDENCE-BASED ANSWER

A/ Yes, according to studies with some limitations. Calcium supplements with or without vitamin D increase the risk of myocardial infarction (MI), with numbers needed to harm (NNH) over 5 years of 69 to 240 (strength of recommendation [SOR]: **B,** meta-analyses of randomized controlled trials [RCTs] that evaluated a predominantly older female population and were limited by study designs).

Calcium supplements with or without vitamin D may increase the risk of stroke, with an NNH over 5 years of 283 (SOR: **B,** meta-analyses of RCTs).

Calcium supplementation, but not a diet rich in calcium, also increases the risk of renal calculi, with an NNH over 7 years of 272 (SOR: **B,** RCT and a cohort study, which also evaluated a predominantly older female population).

Evidence summary

A meta-analysis of 11 randomized, double-blinded placebo-controlled studies assessed the relationship between calcium supplements and the risk of cardiovascular events.[1] A total of 20,071 predominantly female patients (83%) with a mean age of 72 years (range, 51-77 years) received ≥500 mg elemental calcium per day for at least 1 year. Median follow-up was 3.6 to 4 years. Five studies provided individual patient data and all 11 provided trial-level data.

In the 5 studies contributing patient data, women taking calcium supplements had an increased incidence of MI (hazard ratio [HR]=1.31; 95% confidence interval [CI], 1.02-1.67; *P*=.035) with an NNH of 69 over 5 years of calcium supplementation. The trial-level data, from 11 trials with 11,921 patients, also showed an increased incidence of MI in women taking calcium (relative risk [RR]=1.27; 95% CI, 1.01-1.59; *P*=.038). Neither the patient data nor the trial-level data demonstrated a significant increase in strokes.

Limitations of this meta-analysis include the fact that none of the trials was designed to address the risk of cardiovascular disease; in addition, some studies assessed outcomes by patient self-report, raising the possibility of information bias.

Some studies also show an increased stroke risk

The Women's Health Initiative (WHI) study initially reported no increase in cardiovascular risk among women who received calcium and vitamin D supplements, but it didn't take into account whether women were already taking calcium or vitamin D at the time of randomization.[2] Re-analysis of the 16,718 women (mean age 62.9 years) randomized to calcium and vitamin D and not taking calcium supplements before the study found a statistically significant increase in the risk of MI or revascularization (HR=1.16; 95% CI, 1.01-1.34; *P*=.04).[3]

A meta-analysis of these findings and 2 additional RCTs (88% of subjects were female) comparing calcium and vitamin D supplementation with placebo found an in-

creased risk of MI or stroke (RR=1.16; 95% CI, 1.02-1.32; *P*=.02).

Another meta-analysis that examined the WHI data and 5 placebo-controlled studies of calcium or calcium and vitamin D supplementation (82% of subjects were female) found an increased risk of MI, with NNHs over 5 years of 240 for MI (RR=1.26; 95% CI, 1.07-1.47; *P*=.005), 283 for stroke (RR=1.19; 95% CI, 1.02-1.39; *P*=.03), and 178 for the composite of MI or stroke (RR=1.17; 95% CI, 1.05-1.31; *P*=.005).[3] The number needed to treat with calcium (with or without vitamin D) for 5 years to prevent one fracture was 302. The conclusions of this study were limited by post hoc and subgroup analyses.[4]

These studies did not address dietary sources rich in calcium. Dietary calcium results in lower peak serum levels than supplementary calcium, with less potential for adverse effects.[3]

Supplemental, but not dietary, calcium raises the risk of kidney stones

To assess the risk of renal calculi, the WHI randomized 36,282 postmenopausal women to calcium with vitamin D or placebo. Calcium and vitamin D increased the risk of renal calculi (HR=1.17; 95% CI, 1.02-1.34), with an NNH of 272 over 7 years.[5]

In a prospective cohort study of 91,731 women with 12-year follow-up, supplementary calcium was associated with an increased risk of kidney stone formation (RR=1.2; 95% CI, 1.02-1.41), whereas high dietary calcium was linked to a lower risk.[6]

Recommendations

The Institute of Medicine's (IOM's) recommended dietary allowance for calcium from diet plus supplements is 1000 mg a day for women until 50 years of age and no more than 1200 mg a day for women older than 50 years. The IOM advocates a maximum calcium intake of 2000 mg a day for women in both age groups because of the increased risk of kidney stones.[7] JFP

Calcium supplements with or without vitamin D increase the risk of myocardial infarction and may also raise the risk of stroke.

References

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