Calcium Supplements May Increase CVD Risk

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TORONTO – Calcium supplements appear to cause more harm than good, according to a meta-analysis of 28,000 participants in nine trials that includes a new analysis of more than 16,000 participants in the Women's Health Initiative, but the reanalysis has raised concerns among the WHI's original investigators.

"We calculate that for every 1,000 people treated with calcium for 5 years, it will lead to four additional myocardial infarctions, four additional strokes, and two additional deaths, while preventing three fractures," Dr. Ian R. Reid said.

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Major Finding: People taking a calcium supplement showed a statistically significant 24% excess relative risk for MI, a 15% excess relative risk for stroke, and a 16% excess relative risk for MI or stroke.

Data Source: Meta-analysis of nine studies that compared calcium supplements with placebo in a total of more than 28,000 people.

Disclosures: Dr. Reid said that he had no relevant disclosures.

"I don't prescribe calcium supplements to anyone anymore for preventing bone fractures. People should get calcium from their diet," said Dr. Reid of the University of Auckland, New Zealand. He speculated that a calcium supplement, even at a relatively modest dose of 500 mg, produces a "borderline hypercalcemia" that persists for several hours and raises the risk for MI or stroke, the same way that people in the highest quartile for normal blood calcium levels have an increased risk for cardiovascular disease events.

But the researchers who ran the Women's Health Initiative (WHI) study questioned the legitimacy of the new analysis beyond a hypothesis-generating exercise.

"The WHI investigators have concerns about the reanalysis and whether omitting the subgroups with favorable results is appropriate," said Dr. JoAnn E. Manson of Harvard University and Brigham and Women's Hospital, both in Boston, and a WHI coinvestigator.

Dr. Reid and his associates initially reported that calcium supplement use was linked with a statistically significant 27% and 31% relatively increased risk for MI in two separate meta-analyses published online last July (BMJ 2010;341:c3691).

To further explore the impact of calcium supplements on cardiovascular risk, they reanalyzed data collected in a WHI study of more than 36,000 postmenopausal women randomized to receive a daily supplement with 500 mg calcium plus vitamin D or placebo. The original report from the WHI investigators showed that the calcium plus vitamin D did not significantly increase or decrease coronary or cerebrovascular risk in generally healthy postmenopausal women during 7 years of treatment (Circulation 2007;115:846-54).

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DR. REID

But at baseline, more than 19,000 (54%) of the women in the study reported using a calcium supplement on their own, and at the end of the study 69% reported the practice, Dr. Reid said. To address the possible confounding, he focused on the 16,718 women in the WHI study who reported not using a personal calcium supplement at entry.

In this subgroup, the MI rates ran 2.5% in women randomized to calcium supplements and 2.0% in the placebo arm, a 22% relative increase that was statistically significant. The rate of MI or stroke ran a relative 16% higher among the women taking calcium, which was also statistically significant. The results showed no significant effect of calcium supplementation on stroke rate, Dr. Reid said.

But if Dr. Reid's analysis did not start with a prior hypothesis, this finding can only be considered hypothesis generating, not hypothesis testing, Dr. Manson said in an interview. "Many subgroups were tested in the WHI, and some would be expected to show significant effect modification by chance," she pointed out.

When data from the WHI subgroup that did not use personal calcium supplements at baseline were added to the meta-analysis, the results showed that those who did take supplements had a 24% relative excess of MIs, a 15% relative excess of stroke, and a 16% relative excess of MI or stroke, Dr. Reid reported. ■