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Calcium supplements boost heart-attack risk: Meta-analysis

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Auckland, NZ - The use of calcium supplements without coadministered vitamin D is associated with an increased risk of MI [**1**]. The finding, from a meta-analysis encompassing 15 randomized trials and up to 11 921 participants, warrants a reassessment of the role of calcium supplements in the management of osteoporosis, researchers report online July 29, 2010 in *BMJ*.

Most guidelines for the prevention or treatment of osteoporosis recommend the use of calcium supplements, despite the fact that they reduce the risk of fracture only marginally, write **Dr Mark J Bolland** (University of Auckland, New Zealand) and colleagues.

Studies have yielded conflicting results about their use, with some observational studies suggesting that high calcium intake is protective against vascular disease, and others showing that calcium supplements speed vascular calcification and increase mortality in patients with kidney failure and increase cardiovascular events and MI in women.

Senior author **Dr Ian R Reid** (University of Auckland) told **heartwire** that women should discuss the finding from his study with their doctors, but that in most cases, "discontinuation of calcium would seem appropriate."

The researchers had previously found an adverse effect from calcium supplements in a clinical trial, which they published in *BMJ* in 2008 [**2**], Reid explained. They repeated electronic database searches in March of this year to consolidate those findings.

Their current meta-analysis looked at randomized trials of calcium supplements that supplied at least 500 mg/day of elemental calcium vs placebo. Each of the trials lasted for at least a year and had at least 100 participants with a mean age of 40 years or older. Cardiovascular outcomes were obtained from self-reports, hospital admissions, and death certificates.

In a combined analysis of the five studies that had contributed patient-level data, the investigators found that calcium supplements were associated with about a 30% increase in the incidence of MI (hazard ratio 1.31; 95% CI 1.02-1.67; p=0.035) and smaller, nonsignificant increases in the risk of stroke and mortality.

The findings were consistent across trials, and the risk of MI with calcium supplements tended to be greater in those with higher dietary calcium intake. The MI risk was independent of age, sex, and type of supplement.

A similar analysis of 11 trials that contributed trial-level data showed a 1.27 relative risk of MI (95% CI 1.01-1.59; p=0.038) associated with calcium supplements.

"Clinicians should tell their patients that, for most older people, the risks of calcium supplements outweigh the benefits. Changing to calcium-rich foods may be appropriate," Reid said.

Calcium supplements causing heartburn, not MI?

In an editorial accompanying the article [3], **Dr John Cleland** (Castle Hill Hospital, Kingston upon Hull, UK) and colleagues wonder why calcium supplements should increase cardiovascular risk, as found in this meta-analysis. "Accumulation of calcium in the arterial wall leading to reduced compliance would be expected to take years, but the increased risk of myocardial infarction reported by Bolland and colleagues occurred early after calcium supplementation (median follow-up of 3.6 years)."

Cleland et al suggest that the increased risk of MI may not be a true effect, because the increased risk of MI was not accompanied by an increase in mortality. "Calcium supplements could simply be causing gastrointestinal symptoms that could be misdiagnosed as cardiac chest pain," they write, adding that even if the supplements are safe, the neutral effect on mortality "casts doubt on whether they are effective prophylaxis for fractures."

Until more becomes known about the best way to prevent osteoporotic fractures, the editorialists conclude that "patients with osteoporosis should generally not be treated with calcium supplements, either alone or with vitamin D, unless they are also receiving an effective treatment for osteoporosis for a recognized indication." They add that research on whether such supplements are needed in addition to effective osteoporosis treatment is "urgently required."

Dr John Schindler (University of Pittsburgh Medical Center, PA), who isn't a coauthor of the study from Bolland et al, told **heart*wire*** that the increased MI risk in the study, although quite modest, is concerning because of the large numbers of people who take calcium supplements. He also questioned whether vascular calcifications could be the cause, because of the trials' relatively short follow-up times.

Gender differences may be important

For Schindler, research into gender differences may yield answers to the increased risk of MI seen in this meta-analysis.

"In this analysis, 88% of the participants were women, and we know that cardiovascular disease in women is radically different from cardiovascular disease in men. The same holds true for cerebrovascular disease. There is something we need to get at, and at this point, no one has really been able to do so."

Schindler also said that the real risk of MI appeared to be in people who took calcium supplements on top of high levels of dietary calcium. "I think the safest thing to tell your patients right now is if you can get your dietary calcium from good dietary sources, such as yogurt, sardines, and skim milk, that potentially might be all you need to ward off the risk of osteoporosis. Then we don't have to deal with this increased cardiovascular risk."

He added that it is important to consider the potential safety concerns along with the benefits of bone health. "The benefits of calcium supplementation in older women with a low risk of fracture may not outweigh the potential cardiovascular risk."

Finally, Schindler noted the absence in the meta-analysis of the **Women's Health Initiative**, a large study that looked at the role of calcium supplementation with vitamin D in reducing osteoporotic fracture. "There are a lot of data that show that vitamin D is protective from a cardiovascular standpoint. They excluded studies with vitamin D probably because they are trying to isolate one variable. They didn't want to cloud the picture."

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