

Editorial

Calcium Supplements and Heart Disease

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Calcium supplements are widely used in the United States and other developed nations traditionally to avoid osteopenia and its complications, but now often given along with vitamin D supplementation, for maintenance of optimum health for other physiologic processes [1-3]. Concern has been expressed that calcium supplementation may increase the risk of atherosclerotic vascular disease [4,5]. The data is conflicting.

The controversy started with a secondary analysis of a randomized placebo controlled trial of calcium supplements versus placebo in post menopausal women for 5 years, which showed a statistically significant increase in MI. The composite end point of myocardial infarction (MI), stroke or cerebrovascular accident (CVA), or sudden death was higher in calcium group ($P=0.008$), relative risk was 1.66 [4]. When the events were attempted to be adjudicated using a national registry, statistical significance was no longer found. The baseline characteristics of the participants in this study were not adjusted for cardiovascular risk, nor was there adequate documentation for concomitant cardiovascular medications.

Secondly, a meta-analysis of 11 studies showed that allocation of calcium supplements (>500 mg/day for more than a year) was associated with increased risk of MI, and that calcium supplementation was associated with 30% increase in incidence of MI and smaller non-significant increase in risk of CVA and death [5]. None of the trials had CV events as the primary end points, and data on CV events were not gathered in a standardized manner. Incomplete or no data on CV outcomes were available in 7 trials, comprising about 15% of participants. None of the trials were designed to have the baseline characteristics of the subjects equalized, in terms of cardiac risk factors. The trials did not have standardized information about the use of statins, ACE inhibitor therapy or previous history of coronary artery disease (CHD).

The Women's Health Initiative trial, another randomized controlled study, did not show any concerning cardiovascular risk from calcium supplements. The trial was a randomized controlled trial (RCT) of calcium (500 mg) plus Vitamin D (200 IU), twice daily versus placebo in 36,282 post menopausal female, 50 to 79 years at 40 clinical sites, where CVD was a pre-specified secondary efficacy outcome. This study revealed that calcium/vitamin D supplementation neither increased nor decreased the risk for CHD or stroke, in general healthy postmenopausal women throughout the

7-year duration of this randomized trial [6]. A limitation of the trial was that women in the placebo group were allowed to continue their own calcium supplements, and personal use of calcium supplement at randomization could have influenced the effect of randomization to calcium and vitamin D on the risk of cardiovascular events.

A prospective cohort study of 34,486 postmenopausal Iowa women, 55-69 years old and without a history of ischaemic heart disease, was analyzed to investigate whether greater intakes of calcium, vitamin D or milk products may protect against ischaemic heart disease mortality. 8 year follow up suggested that among postmenopausal women, the risk of dying of ischaemic heart disease may be reduced by consuming relatively high levels of calcium. There was an estimation of statistically significant 33% reduction in risk for persons in the highest quartile of total calcium intake (i.e. high whether due to diet, supplements or both) [7]. Limitation of the study was that the duration of supplemental vitamin and mineral use was not known.

Finally, a recent publication was done to evaluate the risk and vascular hospitalization and mortality data from a 5-year randomized, controlled trial of calcium carbonate, and 4.5 years of post-trial follow-up was undertaken. This study used data from a published 5-year randomized, double-blinded, placebo-controlled trial. The participants were 1460 women aged 75 years at baseline recruited from the general population, and randomized to receive 1200 mg of calcium carbonate daily, or an identical placebo. In this intent to treat analysis, the intervention group did not have a higher risk of death or first-time hospitalization from atherosclerotic vascular disease in the 5-year RCT compared to placebo. This trial provides compelling evidence that calcium supplementation of 1200 mg daily does not significantly increase the risk of atherosclerotic vascular disease in elderly women [8].

In summary, when patients are randomized with appropriate risk factors for cardiac health, there is no compelling evidence that the calcium supplementation increase the rate of major cardiovascular events.

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