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Effect of calcium supplements on risk of myocardial infarction and cardiovascular events

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Abstract

In this report we will be discussing the effect of calcium supplements on risk of myocardial infarction and cardiovascular events, 15 studies were included. Overall, 190 potentially relevant reports of studies were identified from the initial searches, but only the 15 studies were eligible for analysis. Thirteen studies compared calcium supplements with placebo, one study had a 2×2 factorial design allowing comparison of calcium with placebo and calcium plus vitamin D with vitamin D,28 and one study compared calcium plus alendronate with alendronate.[1]

Introduction

Osteoporosis is a major cause of morbidity and mortality in older people. Calcium supplements marginally reduce the risk of fracture[2], and most guidelines recommend adequate calcium intake as an integral part of the prevention or treatment of osteoporosis[3]. Consequently, calcium supplements are commonly used by people over the age of. Observational studies suggest that high calcium intake might protect against vascular disease[4], and the findings are consistent with those of interventional studies of calcium supplements that show improvement in some vascular risk factors. In contrast, calcium supplements accelerate vascular calcification and increase mortality in patients with renal failure, in both dialysis and predialysis populations[5]. Furthermore, a five year randomized controlled trial of calcium supplements in healthy older women, in which cardiovascular events were prespecified as secondary end points, recently reported possible increases in rates of myocardial infarction and cardiovascular events in women allocated to calcium. We carried out a meta-analysis of cardiovascular events in randomised trials of calcium supplements.[2]

Methods

Study selection

We included studies if they were randomised, double blind, placebo controlled trials; elemental calcium was administered at a dose of ≥500 mg/day; the participants' mean age at baseline was more than 40 years; 100 or more participants were randomised; participants of either sex were studied; and the trial duration was more than one year. We excluded trials concerning calcium and vitamin D given together with a placebo comparator (trials were only eligible if vitamin D was given to both intervention and control groups, because vitamin D supplementation has been associated with decreased mortality17); trials in which calcium was administered in the form of dietary modification or a complex nutritional supplement; and trials in which most participants had a major systemic disease other than osteoporosis.[2]

Discussion

We invited the lead author of each eligible study to provide patient level data on cardiovascular events that occurred during the study irrespective of whether the participant was still taking the trial drug. When such data were not available we requested summary data at trial level. We obtained patient level data on cardiovascular outcomes for five studies, and partially complete trial level data for six. No data were available for four studies because the original records were no longer available and cardiovascular events were not previously reported,18 20 or no cardiovascular data were available.23 26 Thus, patient level data on cardiovascular outcomes were available for 63% of participants in the 15 eligible studies, complete trial level data for 85% of participants, and at least partially complete trial level data for 93% of participants. Basic demographic and other trial related data were either supplied by the lead authors (or nominated deputies) or extracted from the original publication by an investigator .

End points : The prespecified primary end points were time to first myocardial infarction, time to first stroke, and time to first event for the composite end point of myocardial infarction, stroke, or sudden death. The secondary end point was time to death (all cause mortality).[7]

Results

Results 15 trials were eligible for inclusion, five with patient level data (8151 participants, median follow-up 3.6 years) and 11 with trial level data (11 921 participants, mean duration 4.0 years). In the five studies contributing patient level data, 143 people allocated to calcium had a myocardial infarction compared with 111 allocated to placebo

(hazard ratio 1.31, 95%). Non-significant increases occurred in the incidence of stroke ,the composite end point of myocardial infarction, stroke, or sudden death, and death. The meta-analysis of trial level data showed similar results: 296 people had a myocardial infarction (166 allocated to calcium, 130 to placebo), with an increased incidence of myocardial infarction in those allocated to calcium (pooled relative risk 1.27, 95% confidence interval 1.01 to 1.59, P=0.038).

Conclusion

Calcium supplements (without coadministered vitamin D) are associated with an increased risk of myocardial infarction. As calcium supplements are widely used these modest increases in risk of cardiovascular disease might translate into a large burden of disease in the population. A reassessment of the role of calcium supplements in the management of osteoporosis is warranted.

References

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