

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Calcium supplementation and cardiovascular risk

Calcium supplementation is recommended in postmenopausal women when dietary intake falls short of the recommended daily intake of 1300 mg. Calcium is required for bone health and with adequate vitamin D and appropriate exercise is essential in reducing the risk of osteoporosis. Calcium combined with vitamin D supplementation has been demonstrated to decrease hip and other nonvertebral fracture risk, particularly in aged care residents.

The results of observational studies suggest calcium supplementation may reduce vascular disease risk. However, the results of a New Zealand trial (recently published in the British Medical Journal on February 2, 2008) suggest calcium supplementation in healthy postmenopausal women may increase myocardial infarction (MI) risk. The original intention was to assess the effects of calcium supplementation in postmenopausal women (> 5 years postmenopausal and over 55 years of age) on bone mineral density (BMD) and fracture risk over a period of five years. Women were excluded if they were taking osteoporosis drug therapy, calcium supplements, if serum 25-hydroxyvitamin D (25-OHD) levels were <25 nmol/L or if they had any major ongoing disease. Participants had a mean age of 74 years and were randomized to 1000 mg/day of calcium (as citrate salt) or placebo.

According to self-reported data, women in this study who were receiving calcium had a significant increase in MI risk and the risk of the composite endpoint of MI, stroke, TIA or sudden death compared to placebo. However, when additional cardiovascular (CV) events identified on the national database of hospital admissions in NZ were added to the self-reported events, the difference between the calcium and placebo groups was not significant.

Further difficulties with the interpretation of this trial are:

- although CV events were a pre-specified secondary outcome, many of the subsequent analyses were designed and undertaken post-hoc, as such the results are hypothesis generating and do not represent cause and effect;
- it is uncertain if baseline characteristics of the groups differed, especially with respect to CV risk, as statistical analysis was not reported in the published paper and thus it is not possible to determine whether these influenced the results for certain subgroups (e.g. smokers versus never-smokers);
- serum 25-OHD levels, which influence active absorption of calcium and low vitamin D levels may be associated with increased vascular risk, were not reported.

This research highlights the difficulty in accurately identifying potentially rare adverse effects, and balancing established benefit with unexpected and unconfirmed harm. Given current information, these results do not mandate a change in practice of encouraging postmenopausal women to achieve adequate calcium intake, via diet and/or supplementation, in combination with appropriate exercise and adequate vitamin D, to reduce the risk of osteoporosis and fracture.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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