

# 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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## High dose Vitamin D supplementation

Vitamin D<sub>3</sub> deficiency is associated with muscle pain and weakness, fatigue, reduced bone mineral density and an increased risk of falls and fractures. Vitamin D<sub>3</sub> levels decline with advancing age, presumably due to reduced sun exposure and cutaneous synthesis, and impaired renal function. The recommended daily intake to prevent deficiency in Vitamin D<sub>3</sub> replete patients with minimal sunlight exposure is 400 IU for those aged 51-70 years and 600 IU for those >70 years. Patients in residential care may require higher intakes.

Vitamin D<sub>3</sub> supplementation, usually in combination with calcium, is used in the treatment of osteoporosis and to reduce the risk of falls and fractures amongst high risk elderly patients. However, the evidence is inconsistent. A 2009 Cochrane review concluded that Vitamin D alone is unlikely to prevent fracture, but co-administration of calcium may reduce hip fractures in frail elderly people in residential care. Evidence suggests that at least 700 IU/day of Vitamin D<sub>3</sub> may reduce the relative risk of falls by 19 – 26% compared to calcium alone or placebo.

### *High dose formulations*

High dose Vitamin D<sub>3</sub> formulations are commonly used to improve adherence or to rapidly correct Vitamin D<sub>3</sub> deficiency. In Australia these formulations are available on private prescription and are usually prepared by compounding pharmacies. Early trials using Vitamin D<sub>2</sub> found benefit but were uncontrolled and unblinded. In 2003 a randomised double-blind controlled trial in 2686 elderly, community-dwelling men and women found a reduction for first hip, wrist, forearm or vertebral fracture in those taking Vitamin D<sub>3</sub> 100,000 IU orally every 4 months (RR 0.67, 95% CI 0.48-0.93, P=0.02). This trial did not assess calcium intake and falls.

In a recent Australian double-blind trial, 2256 community-dwelling women aged  $\geq 70$  years at high risk of fracture were randomised to receive an oral vitamin D<sub>3</sub> 500,000 IU annually or placebo for 3-5 years. Women taking Vitamin D<sub>3</sub> were more likely to fall (RR 1.15; 95% CI, 1.02-1.30; P=0.03) and more likely to have a fracture (RR 1.26; 95% CI 1.00 – 1.59; P=0.02). Falls and fractures were more common in the first 3 months after dosing although for fractures this was a non-significant trend. This is the first trial to suggest an association between Vitamin D<sub>3</sub> therapy and increased falls risk. The possible mechanism is unclear; one suggestion is that a rapid improvement in myopathy and activity levels following this very high dose may be implicated.

Further trials are required to provide reassurance on the safety and efficacy of commonly used high dose Vitamin D<sub>3</sub> regimens in both general and high risk populations.

This E-Bulletin is based on work by Karin Nyfort-Hansen, Senior Clinical Pharmacist, RGH

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