The Role of Vitamin D in Falls Prevention: an Overview

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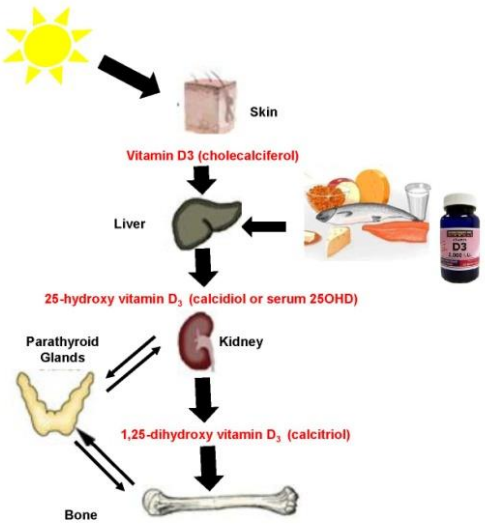
Introduction

Falls are a major health issue with one in three community dwelling people aged 65+ yrs and one in every two people living in residential aged care facilities falling annually [1, 2]. Vitamin D deficiency is an identified risk factor for falls in older people and this review summarises the evidence around vitamin D supplementation and fall prevention for this group.

Vitamin D is a steroid hormone and most cells in the body including those within muscle and nervous tissues have receptors for Vitamin D ([3]. Vitamin D plays a role in calcium and phosphate metabolism and is important for bone and muscle function ([4]. The main source of Vitamin D is from exposure to sunlight. Vitamin D is synthesised from 7-dehydrocholesterol in the skin following exposure to the ultraviolet B radiation of the sun. This is metabolised in the liver to 25-hydroxy vitamin D, the metabolite most commonly measured in blood tests for Vitamin D [5]. However, 25-hydroxy vitamin D is further metabolized by the kidney to produce the active form of vitamin D (1,25 dihydroxy vitamin D_3 or calcitriol) as shown in Figure 1.

Figure 1 Vitamin D synthesis (adapted from http://rickets.stanford.edu/)



The Institute of Medicine (IOM), the health arm of the National Academy of Sciences (USA), has defined a serum level of 25 hydroxyvitamin D of 50nmol/L (20ng/ml) or above as adequate with levels below 25nmol/L (10ng/ml) considered as deficient. However, there is some debate about the minimum level of serum Vitamin D required for bone health with minimal levels recommended between 50 and
75nmol/L ([6, 7].

Studies in Australia have found Vitamin D insufficiency (levels below 50nmol/L) to be around 46% in women and 22% in men over 65 years, increasing to 57% for women and 28% for men over 75 years

[8]. There is seasonal variation in Vitamin D levels with the highest levels found in summer and the lowest levels found following winter, i.e. September [9].

Vitamin D and falls reviews and meta-analyses

Several systematic reviews and meta-analyses, including gold standard Cochrane reviews, have been undertaken to determine the effects of Vitamin D supplementation on falls and some of these have included fracture data. Primary findings of these reviews are presented in Table 1.

The most recent Cochrane review on interventions for preventing falls in the community [10], concluded that Vitamin D supplementation did not reduce the rate of falls in this group as a whole. However, a subgroup analysis undertaken on participants who had low vitamin D levels at enrolment demonstrated a 43% reduction in the rate of falls (RaR 0.57; 95%CI 0.37 to 0.89) in these participants (see Table 1).

The recently updated Cochrane review [11] on interventions for preventing falls in care facilities and hospitals reported that average Vitamin D levels in these settings were low or very low. The review concluded that in care facilities, Vitamin D supplementation reduced the rate of falls by 37% (RaR 0.63, 95% CI 0.46 to 0.86). One study on vitamin D supplementation conducted in an acute geriatric unit was also included in this review. In this setting, there was no effect of Vitamin D supplementation on the risk of falling: a finding undoubtedly influenced by the relatively short intervention period (median length of stay 30 days) for this type of intervention.

A third Cochrane review of Vitamin D supplementation [12] in older women living in institutional care found a significant reduction in hip fractures (RR =0.84, 95% CI 0.73 to 0.96). The authors, concluded, however, that it is not possible to determine whether Vitamin D on its own can prevent hip fractures as most of the studies also included calcium supplementation.

Further systematic reviews have addressed other important aspects of vitamin D supplementation. Two systematic reviews have found that a reduction in falls and/or fractures is dose dependent, i.e. doses of at least 800 IU per day are required to prevent falls and fractures [13, 14]. Other reviews have pointed out that the efficacy of interventions might depend on the type of supplementation provided. For example, it has been shown that Vitamin D_3 cholecalciferol (the most commonly prescribed form of vitamin D in Australia) is more potent than vitamin D_2 ergocalciferol in both raising and maintaining serum 25 Hydroxyvitamin D and produces 2-3 fold greater storage [15]. To complement most reviews that have used “intention to treat” data, Bischoff Ferrari et al [16] conducted an “as treated” analysis in their systematic review and concluded that adherence to the supplementation (i.e. actually taking the vitamin D tablets) was also crucial for a reduction in falls.

With regard to mechanisms as to why vitamin D may prevent falls, studies have shown that vitamin D supplementation improves neuromuscular and psychomotor performance in older people living in both the community ([17-19] and residential aged care facilities [18, 20].

Finally it is worth noting that a well conducted Australian study found very high single annual doses of Vitamin D (500,000 IU D_3 administered orally in autumn or winter) provided over 3-5 years increased the risk of both falls and fractures [21]. The mechanisms underlying this unexpected finding are unclear but suggest that high single annual dose supplementation should be avoided.

Discussion

One of the main limitations of the meta-analyses undertaken is the heterogeneity of the trials included. This is reflected in the inclusion of both high and low quality trials, variability in dose prescribed (ranging from 200 to 1200 IU per day or high doses given monthly or yearly), the form of Vitamin D (D_2 versus D_3) provided and the variable addition of calcium as part of the intervention. Some studies have also had poor definitions of falls and inconsistent collection of falls data. There is also variation in adherence to treatment (68-100%) with lower rates of adherence reported when calcium is included (Rizzoli et al 2009). Another issue relates to the proportion of participants in included studies that are actually vitamin D deficient. As could be expected, the beneficial effect in relation to fall prevention has primarily been evident in those with lower levels of Vitamin D. It has been shown that there is a correlation between the initial severity of vitamin D insufficiency and its effect on physical performance improvement [4].

Despite these methodological limitations, a number of key findings emerge. First, vitamin D supplementation is particularly beneficial for people living in residential aged care facilities where fall risk is high and vitamin D deficiency is widespread. In this setting falls can be reduced by 72% (800 IU daily for 5 months, mean age 89 years) [20]. Second, vitamin D supplementation also prevents falls in frail or primarily house bound older people living in the community who are vitamin D deficient. Third, vitamin D supplementation has very few side effects. Therefore, unless contraindicated, vitamin D should be routinely prescribed for the above groups. It is also worth noting that for people with significant renal impairment, it may be necessary to administer the active form of vitamin D – calcitriol.

A recent position statement by Osteoporosis Australia (OA) recommends that vitamin D supplementation be offered to older or disabled people in residential care and community dwelling older people admitted to hospital as these groups are likely to be at high risk of vitamin D deficiency [5]. OA recommends a daily dose of vitamin D supplementation of 600IU (15µg) for those ≤ 70 years, 800 IU (20 µg) for those >70 years and 1,000IU (25 µg) for older people who are housebound or reside in residential aged care facilities along with adequate calcium (1,000-1,300mg/day) preferably from their diet. The recommendation for reducing fracture risk in older people is 1,000 IU (25 µg) per day [5, 22].

Osteoporosis Australia has produced a range of publications on Vitamin D for professionals and consumers including information on sun exposure for bone health. These can be accessed at http://www.osteoporosis.org.au/about/about-osteoporosis/information-to-download/

A final issue relates to compliance, in that many older people are on a number of medications and are reluctant to take multiple pills. This barrier can be overcome by the administration of inexpensive vitamin D drops in weekly or monthly doses. Alternatively, compounding pharmacists are able to produce 50,000IU tablets for monthly prescription.

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Table 1 Summary of Reviews and Meta-analysis of Vitamin D and Falls prevention studies

Author and year	No of studies included	No of participants (mean age, % female)	Vitamin D (dose, formulation and duration of treatment)	Outcomes of Study
Gillespie et al 2012 (Cochrane Review)	14 RCT (8 included calcium)	28,135 (76 years, 79% female)	Vitamin D_3 (200-2,000 IU daily, to 100,000 IU every 4 months Treatment duration varied from 8 weeks to 5 years Vitamin D_2 (1,000 IU daily to 500,000 IU yearly) Some studies included Calcium daily up to 1,000mg	No statistical difference in rate of falls RaR 1.00 (95% CI 0.90 – 1.11), 9324 participants in 7 trials. Risk of falling RR 0.96 (95% CI 0.89 – 1.03), 26,747 participants, 13 trials. In a subgroup analysis of trials with participants with lower Vitamin D levels there was a reduction in rate of falls and risk of falling. RaR 0.57 (95%CI 0.37 to 0.89), 260 participants, 2 trials RR 0.70 (95%CI 0.56 to 0.87), 804 participants, 4 trials.
Cameron et al 2012 (Cochrane Review)	5 RCT (Care Facilities) 1 RCT (Acute Aged Care Ward)	4603 (85.6 years, 83 % female) 205 (83 years, 59% female)	Vitamin D_3 (400-800 IU daily, with or without calcium 1200mg) Vitamin D_2 (1000 -1100 IU daily) 3-24 months treatment duration 800IU Vitamin D3 + 1200 mg calcium daily until discharge (median length of stay 30 days)	Significant reduction in the rate of falls RaR 0.63, 95% CI 0.46 to 0.86 (5 trials, 4603 participants. No significant reduction in the risk of falling RR 0.99, 95% CI 0.90 -1.08, 5 trials, 4603 participants. No significant effect on risk of falling RR 0.82, (5% CI 0.59 – 1.14.
Bischoff-Ferrari et al 2009	8 RCT (7 included	2426 (80 years, 81% female)	Vitamin D_3 (5 studies) Vitamin D_2 (3 studies)	Reduction in falls of 19% (pooled RR 0.81 (95% CI 0.71- 0.92)

Author and year	No of studies included	No of participants (mean age, % female)	Vitamin D (dose, formulation and duration of treatment)	Outcomes of Study
	calcium)		Daily Dose range 200IU to 1,000 IU 2-36 months treatment duration	Non-vertebral fractures reduced by 20% Falls reduction was dependant on : Vitamin D Dose (>700 IU Vitamin D daily)25 OHD levels required >60nmoL (24 ng/mL) for falls reduction >75nmol/L (30ng/mL) for fracture reduction
Kalyani et al 2010	10 studies (7 included calcium 600-1200mg daily) + 7 studies included for post hoc analysis	2,932 (79 years, mostly female)	Vitamin D_3 (6 studies) Vitamin D_2 (3 studies) Alfacalcidol (1 study) Daily dosage 200- 800IU 1-36 months treatment duration	Reduction of falls of 14% (RR = 0.86, 95% CI 0.79-0.93) Falls reduction was dependent on: > 800 IU Vitamin D daily > 6 months treatment Use of Vitamin D_3
Murad et al 2011	26 RCT (14 included calcium 500-1200mg daily)	45,782 (76 years, 78% female)	Vitamin D_3 (11 studies) Vitamin D_2 (8 studies) Daily dosage 400 -1,000 IU Also included dosages up to 500,000 IU orally annually. 3-62 months treatment duration	Reduction in risk of falls (OR for the risk of suffering at least 1 fall) OR 0.86 (95%CI 0.77-0.96)

OR – Odds Ratio, RaR – Rate Ratio, RR- Relative Risk, Vitamin D_2 – ergocalciferol, Vitamin D_3 – cholecalciferol