November 30, 2012

Edna P. Schwab MD


Background:

Results regarding the relationship of vitamin D intake and fracture reduction have been inconsistent

Seventy five percent of fractures occur in people over 65 y.o. some strategists suggest that Vit D supplementation become universal

One meta-analysis of double blind randomized controlled trials suggest 18% reduction in incidence of hip fracture and 20 % reduction in any nonvertebral fracture at doses of no less than 482 IU/d other meta-analyses suggest that Vit D has no effect on total fracture reduction or may reduce hip fracture by 7 to 16% if combined with calcium regardless of vitamin D dose.

Goal: Current analysis performed to estimate effect of Vit D supplementation according to dose participant used.

Methods:

Identified all double-blind, randomized controlled trials involving persons 65 y.o. and older on oral vitamin d supplementation alone or in combination with calcium compared with a control (placebo or calcium alone) which were published on or before 8/31/2011 that included low trauma fractures. Medline, Cochrane Register and Embase were searched.

12 trials with total of 33,277 participants were included and data for 30,011 participants over 65 y.o were received.

  11 studies had either daily, weekly or every 4 month dose of Vit D
  1 study provided once yearly dose of Vit D
  1 trial was split into study A (vitamin D vs. placebo) and study B (vit D +Ca vs Ca alone).

Variables:

  Adherence to study treatment followed predefined protocol, 7 trials had data available at participant level while 4 did not
  Vit D supplementation outside study protocol was permitted in 5/11, 3
trials had participant level information. Two trials permitted 200 IU Vit D per day or included participants who took less than 400 IU/day. Data on sex and dwelling of participants available for all 12 trials. Fractures verified by medical record review, vertebral fractures were excluded due to lack of consistent documentation.

Outcome Measures

Endpoints were risk of hip and any non vertebral fracture. Analysis compared actual intake of Vit D between treated participants and controls. Subgroup analysis assessed effect of Vit D intake according to age group (<75 y.o., 75-84 y.o., >85 y.o.), type of dwelling (community vs institution), baseline level of 25-OH Vit D (<30 nm/l vs >30 nm/l), additional calcium supplement in treated group (<1000 mg/d or ≥1000 mg/d).

Results

Table 1: Looks at pooled patient characteristics
25 OH Vit D: 24% <30 nm/l
62% <50 nm/l
88% <75 nm/l

Overall 10% reduction in risk of hip fracture in all treatment doses of Vit D (nonsignificant).

Table 2. Significant 30% reduction in incidence of hip fracture at highest actual intake of Vit D (792-2000 IU/d) compared to controls—

No reduction in risk of hip fracture at intake levels <792 IU/day—suggesting a dose response relationship.

7% reduction in nonvertebral fractures with no risk reduction at doses of ≤400 IU/day and 11% reduction at doses >400 IU/day.

Table 3. No Significant interaction between highest intake of vit D and subgroups including age, dwelling, baseline 25 OH Vit D and calcium intake

Discussion:

Study suggests that high intake of Vit D (800 IU) among those over 65 y.o. significantly reduces risk of hip fracture (30%) and nonvertebral fracture (14%). Overall intention to treat analysis there was a non significant reduction of hip fracture (10%) and 7% reduction in nonvertebral fracture. This may underestimate the benefit of
Vitamin D supplementation. The benefit is greatest in the group taking in the highest level of vitamin D.

Previous trials of Vit D supplementation have not shown a benefit due to lower than intended doses of Vit D. Other analyses have suggested that benefits were limited to older persons living in institutions. Current analysis suggest that the benefit in reduction of hip fracture at the highest intake dose occurs in both community dwelling and institutionalized individuals as well as those with very low baseline 25 OH vit D levels.

Data also suggests that the high dose of Vit D combined with the lower dose of calcium supplementation (1000mg/d) may be more beneficial in reducing risk of fracture.

The longer the dosing interval of Vit D, the less benefit on fracture reduction.

Practice Implications

Study supports the IOM recommendation that persons over the age of 65 y.o. receive 800 IU Vit D/d. Supplemental Vit D at high doses (800 IU/d) along with lower doses of Calcium < 1000mg/d have an impact on fracture reduction rate of the hip and nonvertebral areas. A 25 OH Vit D level of >60nmole/l may be most beneficial in reducing risk of fracture (Figure 1).