Vitamin D Supplementation: Preventing Fractures

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INTRODUCTION

Vitamin D is a fat soluble vitamin important for bone health as it promotes calcium absorption, maintains serum calcium and phosphate levels, and enables for normal bone mineralization. The current issue surrounding the screening for vitamin D deficiency focuses on a lack of accepted standards for classification and assessment. Little evidence is available as to when is the appropriate time to begin screening for vitamin D deficiency and if the long term effects of supplementation are beneficial. Vitamin D deficiency is classified differently depending on the organization and the lack of continuity is cause for confusion on who to screen and when to supplement. Low vitamin D levels are associated with increased risk for bone loss and fractures. The purpose of this review is to determine if supplementation of vitamin D is beneficial in preventing fractures and/or osteoporosis.

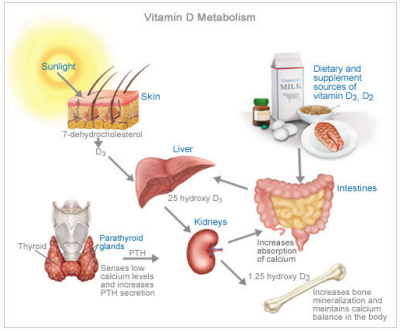


Figure 1. Vitamin D Metabolism retreived from http://plantbaseddietitian.com/tag/bone-metabolism/

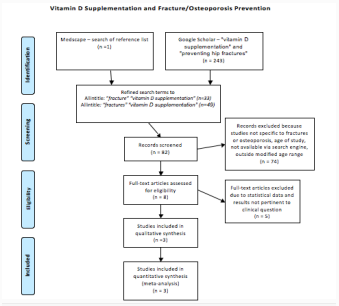
CLINICAL QUESTION

PICO:

- Patient/Population – Patients over the age of 50 years old
- Intervention – Vitamin D supplementation
- Comparison – No supplementation
- Outcome – Preventing bone fractures/osteoporosis

In patients ages 50 and older with vitamin D deficiency, is vitamin D supplementation compared to no supplementation beneficial for preventing fractures/osteoporosis?

METHODS



RESULTS

Study One: **Fracture Prevention with Vitamin D Supplementation – A Meta-analysis of Randomized Controlled Trials.**

Objective: The objective of this study was to estimate the effectiveness of vitamin D supplementation to prevent fractures in adults over the age of 60 years old.

Design: Meta-analysis of 7 double blinded RCTs

Results: Results were stratified first into a hip fracture category and non-vertebral fracture category then into low dose or high dose category. High dose oral vitamin D supplementation appears to reduce the risk of hip and any non-vertebral fractures while low dose vitamin D is not sufficient for fracture prevention.

Table 1. Intention to Treat Analysis -- Hip Fracture Results

Hip Fracture	Relative Risk	Q Test (P-value)
Pooled Data	0.88	0.09 (Heterogeneity)
High Dose (700-800IU/day) NNT = 45	0.74	0.74 (Homogeneity)
Low Dose (400IU/day)	1.15	0.68 (Homogeneity)

Table 2. Intention to Treat Analysis -- Nonvertebral Fracture Results

Nonvertebral Fracture	Relative Risk	Q Test (P-Value)
Pooled Data	0.83	0.07 (Heterogeneity)
High Dose (700-800IU/day) NNT = 27	0.77	0.41
Low Dose (400IU/day)	1.03	0.36

Critique: This meta-analysis had an adequate sample size and pertains to the age of our target patient population. This article was published in 2005 and analyzes studies that were performed over 10 years ago. It also included non-english studies that may not pertain to our patient population because there may be different risk factors for osteoporosis and vitamin D deficiency in other countries.

Study Two: **Calcium plus Vitamin D Supplementation and the Risk of Fractures.**

Objective: The objective of this paper was to assess the primary hypothesis that postmenopausal women randomly assigned to a calcium plus vitamin D supplementation group versus a control group would reduce the risk of fractures, specifically hip fractures or secondarily all fractures.

Design: Double blinded, randomized controlled trial consisting of 36,282 postmenopausal women ages 50-75 recruited from the Women's Health Initiative (WHI) clinical trials

Results: The study showed that bone loss was reduced with the use of calcium w/ vitamin D supplementation but lacked statistical significance to reduce fractures of the hip, vertebra, lower arm or wrist. An increase in renal calculi was noted.

Table 3. Rate of Fracture Summary -- Number of cases (annualized %)

	Calcium + Vitamin D	Placebo	Hazard Ratio (95% CI)
Hip	175 (0.14)	199 (0.16)	0.88 (0.72-1.08)
Clinical Vertebral	181 (0.14)	197 (0.15)	0.90 (0.74-1.10)
Lower arm or wrist	565 (0.44)	557 (0.44)	1.01 (0.90-1.14)
Total	2102 (1.64)	2158 (1.70)	0.96 (0.91-1.02)

Critique: Positive aspect of this article is it had a very large sample size. However, participants were allowed to consume up to 1,000 mg/d of calcium and 600 IU/d of vitamin D as extra supplementation and it was not regulated by the trial and therefore had great risk for skewing data. Like study one, this is an old study published in 2006 and was performed from 1995-2000. Another concern is the participants were recruited from WHI dietary modification and hormone therapy trials. Altered diet and consumption of hormones may affect the absorption of vitamin D and calcium.

RESULTS cont'd

Study Three: **Treatment of Vitamin Insufficiency in Postmenopausal Women - A Randomized Clinical Trial**

Objective: The objective of this research article was to investigate the effects of high and low dose cholecalciferol on total fractional calcium absorption, bone mineral density, and muscle fitness after one year in postmenopausal women with vitamin D insufficiency.

Design: RCT including 230 postmenopausal women ages 75 and younger recruited from local advertisements. Randomized into a high dose cholecalciferol (50,000 IU/d), low dose (800 IU/d), or placebo group. Each group took a white capsule daily and a yellow capsule every 15th day depending on their specified treatment group.

Results: Considerable variability among mean serum 25 (OH)D levels were found between low-dose group, high-dose group and placebo group. Total fractional calcium absorption did increase with high-dose group but decreased with low-dose and placebo groups.

Critique: Small sample size (n=230) is limiting for significance of results; more recent study and good adherence to the study is good (100% across all arms); only recruited from Wisconsin; short follow up of only 1 year (not great for significant results)

DISCUSSION

Table 4. Overall Summary of Included Studies

	Bischoff et al	Jackson et al	Hansen et al
Study population	9,280	36,282	230
Age of participants	≥ 60 yo	50-79 yo	≤ 75 yo
Calcium admin	4 @ 500-1,200 mg/day 3 @ 800 mg/day	1,000 mg/day	600-1,400 mg/day
Vitamin D admin	2 @ 400 IU/day 5 @ 700-800 IU/day	400 IU/day	Low dose – 800 IU/day High dose – 50,000/mo
Duration of study	Meta-analysis – 1960-2005	1995-2005	2010-2014
Length of follow-up	2 yr	7 yr avg	1 yr
Compliance	N/A	~67%	nearly 100%

CONCLUSIONS

The summation of our investigation into vitamin D deficiency and presence of musculoskeletal fractures has proven to be relatively inconclusive. The resulting data from our three studies did not provide any definitive proof that increased vitamin D levels creates significantly better bone health. We do believe there is a positive association between higher doses of vitamin D, with or without calcium, and better bone integrity versus lower doses of vitamin D, with or without calcium. There is an upcoming clinical trial scheduled to begin in January of 2016 titled "Effects of Vit D Fortification on Vit D Metabolite Profiles and Status in Vit D Insufficient Individuals" (ID# - NCT02422784). Hopefully this trial will provide more conclusive evidence of the benefit of vitamin D throughout its research that can provide better clinically applicable recommendations.

REFERENCES

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