Long-Term Care Updates

March 2023

Does Vitamin D Supplementation Provide Benefit in Preventing Fractures?

PharMerica®

By Alyssa Ferrazzo, PharmD

Introduction:

In 2019, there were 178 million new fractures that occurred worldwide and 455 million cases of short-term or long-term symptoms of a fracture.[1] Of new osteoporotic fractures, around 2 million occur in the United States every year.[2] Most fractures are hip fractures and because the risk is higher with age, those most affected are the geriatric population (≥65 years old).[3] Hip and other fractures can lead to an abundance of complications.[4] Hospitalizations can be costly for patients who are commonly on fixed incomes. Disabilities post-fracture can arise, greatly affecting quality of life. Some fractures can even be fatal.[4] People with osteoporosis, low bone mass, or both are at the highest risk for falls leading to fractures.[2] Precautions can decrease fall risk; however, devastating falls leading to fractures are still a significant problem.

For years, researchers have been investigating the impact vitamin D_3 supplementation (cholecalciferol) could have in lowering the incidence of fractures in the elderly population. Currently, vitamin D_3's only FDA-approved indications are prevention of osteoporosis and vitamin D insufficiency and deficiency. Its role as a vitamin D analog involves its active metabolite, 1,25-dihydroxyvitamin D (calcitriol) stimulating calcium and phosphate absorption from the small intestine, promoting secretion of calcium from the bone to the blood, and in turn promoting renal tubule phosphate resorption. This provitamin may support skeletal health and enhance bone mineralization through these mechanisms.[5] Additionally, it is thought to reduce secondary hyperparathyroidism, decrease bone turnover, and may be involved in bone formation.[2]

The following article will review literature regarding vitamin D_3 and its potential benefit of decreased fractures in patients without vitamin D deficiency or osteoporosis.

Clinical Evidence:

In a recently published ancillary study of the Vitamin D and Omega-3 (VITAL) trial, supplemental vitamin D_3 was evaluated to determine if intake would lower the risk of fractures as compared to placebo.[2] The primary endpoints were first incident total, nonvertebral, and hip fractures. A total of 25,871 community-dwelling men and women were randomly assigned to vitamin D_3 2000 units a day (n = 12,927) or placebo (n = 12,944). The average age in both groups was 67 years old (67.1 +/- 7.1), suggesting that most patients were classified as elderly. Most participants were of Non-Hispanic White race (71.3%) with Black participants making up 20.2% of participants. Of note, participants were not selected based on vitamin D level (deficiency), suboptimal bone mass, or diagnosis of osteoporosis. Of those enrolled, 10.3% had a history of fragility fracture with 27.4% and 26.4% having unintentional falls in the past year in the vitamin D_3 and placebo groups, respectively. A similar number of participants (~5%) were currently using osteoporosis medications in each group and approximately 43% were on supplemental vitamin D at baseline. The baseline 25-hydroxyvitamin D level was 30.7 +/- 10.0ng/mL.[2] This value was within the normal ranges of 20 to 40ng/mL and 30 to 50ng/mL (variability is provider preference).[6] The primary endpoint results were similar among both study groups and are shown in Table 1. Researchers concluded that in this randomized, controlled trial, supplemental vitamin D_3 at 2000 units daily did not lower the risk of incident total, nonvertebral, or hip fractures when compared to a placebo among midlife and older adults.[2]

Table 1. Fractures associated with vitamin D or placebo[2]

Confirmed Incident Fractures	Vitamin D Group (N = 12,927)	Placebo Group (N = 12,944)	Hazard Ratio (95% CI)
Total	769 (5.9%)	782 (6.0%)	0.98 (0.89 to 1.08)
Nonvertebral	721 (5.6%)	744 (5.7%)	0.97 (0.87 to 1.07)
Hip	57 (0.44%)	56 (0.43%)	1.01 (0.70 - 1.47)

A 2018 systematic review for the U.S. Preventative Services Task Force investigated whether vitamin D_3, calcium, or combined supplementation influenced the primary prevention of fractures in community-dwelling adults. The studies included English-language randomized-controlled trials (RCTs) or observational studies of supplementation with vitamin D_3, calcium, or both. The final review compiled data from 8 RCTs (n = 47,672) in adults ≥50 years. Study lengths ranged from 3 to 7 years. The main outcome involved finding direct evidence for supplementation with vitamin D_3 or calcium alone or vitamin D_3 combined with calcium in preventing fractures. The vitamin D doses included 300 IU, 400 IU, or 700 IU daily or 100,000 IU every month (after an initial loading dose of 200,000 IU) or every 4 months. The results of this review showed that when compared to placebo, vitamin D supplementation alone (without calcium) decreased total fracture incidence (1 RCT [n = 2,676]; absolute risk difference -2.26% [95% CI, -4.53% - 0.00%]) but did not show significance in hip fractures (3 RCTs [n = 5,496]; pooled absolute risk difference, -0.01% [95% CI, -0.80%. - 0.78%]). Researchers concluded vitamin D supplementation alone was not associated with decreased incidence of hip fractures among community-dwelling adults without known osteoporosis disease, a vitamin D deficiency, or a prior fracture but may have benefits in reducing total fractures.[7]

A 2020 randomized-controlled trial published in The Journal of the American Medical Association (JAMA) looked at the effect of vitamin D supplementation, omega-3 fatty acid supplementation, or a strength-training exercise program on clinical outcomes in older adults (DO-HEALTH). They investigated the effects of these interventions alone or in combination over a period of 3 years in adults 70 years and older. One of the main outcomes was incident rates of nonvertebral fractures. This trial enrolled 2,157 participants with 10.9% taking vitamin D 800 IU or more daily, 40.7% with a vitamin D deficiency (25[OH]D < 20 ng/mL), and 41.9% with a fall in the year prior to enrollment. The vitamin D dosage given to participants was 2000 IU daily. The results showed a nonvertebral fracture incidence rate of 0.04 per person per year in those that received vitamin D and those that did not take the supplementation (99% CI, 0.03 – 0.035; p = 0.79). Vitamin D supplementation in this trial did not show improvements in incidence rates of nonvertebral fractures.[8]

Conclusion:

Currently, most published research presents no additional benefit of vitamin D_3 supplementation in preventing fractures in elderly adults who do not have osteoporosis or a vitamin D deficiency. The literature discussed in this article showed vitamin D_3 supplementation did not decrease the incidence of nonvertebral and hip fractures. There was mixed evidence on the impact on total fractures as one study in the systematic review did mention benefit, but the most recent VITAL trial showed no decreased incidence on total fractures when supplementing with vitamin D. Trials that have shown benefit generally have been low quality and contain confounding variables that limit the results. Vitamin D_3 supplementation is recommended as part of the treatment of osteoporosis, specifically for those receiving pharmacologic treatment for osteoporosis or for those who have subtherapeutic serum levels. At this time, it does not have a recommendation for preventing fractures in geriatric patients without these indications.

References:

1. Wu A, Bisignano C, James SL, et al. Global, regional, and national burden of bone fractures in 204 countries and territories, 1990-2019: A systematic analysis from the Global Burden of Disease Study 2019. *Lancet Healthy Longev*. 2021;2(9):e580-e592.
2. LeBoff MS, Chou SH, Ratliff, KA, et al. Supplemental vitamin D and incident fractures in midlife and older adults. *N Engl J Med.* 2022;387(4):299-309.
3. Hip Fractures Among Older Adults. Centers for Disease Control and Prevention. https://www.cdc.gov/falls/hip-fractures.html. Updated September 20, 2016. Accessed January 17, 2023.
4. Stevens JA and Olson S. Reducing falls and esulting Hip Fractures Among Older Women. Centers for Disease Control and Prevention. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr4902a2.htm. Updated May 2, 2001. Accessed January 17, 2023.
5. Cholecalciferol. In: Lexi-drugs online [database on the Internet]. Hudson (OH): Lexicomp Inc. [updated 16 Dec 2022; cited 22 Jan 2023]. Available from: http://online.lexi.com. Subscription required to view.
6. Medical Tests: 25-hydroxyvitamin D test. The University of California, San Francisco Medical Center. https://www.ucsfhealth.org/medical-tests/25-hydroxy-vitamin-d-test. Updated May 17, 2018. Accessed January 22, 2023.
7. Kahwati LC, Weber RP, Pan H, et al. Vitamin D, calcium, or combined supplementation for the primary prevention of fractures in community-dwelling adults: Evidence report and systematic review for the US Preventative Services Task Force. *JAMA*. 2018;319(15):1600.
8. Bischoff-Ferrari HA, Vellas B, Rizzoli R, et al. Effect of vitamin D supplementation, omega-3 fatty acid supplementation, or a strength-training exercise program on clinical outcomes in older adults. *JAMA*. 2020;324(18):1855-1868.