


Is Supplementation of Vitamin D Beneficial for Fracture Healing? A Short Review of the Literature

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Abstract

There has been a surge of interest regarding the benefits of vitamin D supplementation to prevent fractures. But can it also make them heal more quickly once they have occurred—that is, is supplementation of vitamin D beneficial for fracture healing? We found 13 studies that met our inclusion criteria, 11 of these were performed in animals. Two animal studies showed negative, 2 neutral, and 7 positive results. One clinical case series in humans was inconclusive in our opinion, and one randomized double-blind placebo-controlled trial showed that supplementation of vitamin D₃ and calcium in elderly women with reduced bone mass and a proximal humerus fracture had a positive influence on bone healing. The major weakness of the latter study is low number of participants. A clear statement on the benefits of vitamin D for fracture healing awaits further trials, but all types of fractures in elderly individuals indicate the need for secondary prevention and the implementation of appropriate guidelines concerning falls, vitamin D, and osteoporosis.

Keywords

fracture healing, vitamin D, osteoporosis

Introduction

There has been a surge of interest regarding the benefits of vitamin D supplementation in the elderly. For instance, a meta-analysis by Bischoff-Ferrari et al concluded that with a “higher” dose of oral vitamin D, nonvertebral “fractures should be reduced by at least 20% for individuals aged 65 years or older.”¹ The effect of vitamin D is not limited to bone health, that is, stronger bones are less likely to fracture, as “supplemental vitamin D in a dose of 700 to 1000 IU a day reduced the risk of falling among older individuals by 19%.”² The effect seems to be mediated by improvement of muscle function. These findings were summarized in a clinical recommendation: based on the available evidence for preventing falls and fractures, a general supplementation with at least 800 U/d of vitamin D should be considered in persons aged 60 years or older.³ From an epidemiologic and economic point of view, prevention of falls and fractures in the first place, or reducing morbidity once they have occurred, is an important issue in our ever increasing elderly population.⁴

If vitamin D can prevent fractures, can it also make them heal more quickly once they have occurred—that is, is supplementation of vitamin D beneficial for fracture healing? We performed a short review of the literature to address this issue (with a particular focus on elderly individuals).

Search Method

We searched PubMed on December 14, 2010, using the terms “vitamin D” and “fracture healing” or “bone healing” or “callus formation.” We retrieved a total of 70 publications; 61 were eliminated because of lack of relevance after screening titles and abstracts. Searching the reference lists of the remaining 9 publications, we found an additional 4 articles. By comparison, just using “vitamin D” as a search term, there are 38 780 hits.

Results and Discussion

Is supplementation of vitamin D beneficial for fracture healing? We have to bear in mind that the typical elderly patient with a (hip) fracture has relevant vitamin D deficiency.⁵⁻⁷ The results of our specific literature search are disappointing (compared with the number of publications on vitamin D in general). Although we found 13 studies that met our inclusion criteria

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Table 1. Summary of Animal Studies on the Benefits of Vitamin D for Fracture Healing

Authors	Animal Model	Results
Melhus et al ⁸	Rat model that mimics conditions in elderly women (postmenopausal state combined with vitamin D deficient diets)	Fracture healing was not markedly affected in comparison with control animals (normal diets without vitamin D deficiency)
Einhorn et al ⁹	Rats received various combinations of protein- or mineral-deprived/supplemented diets; the subgroup with “mineral” supplementation also received additional vitamin D	The strength of the fracture callus was dependent on adequate dietary protein; supplementation with vitamin D neither improved nor impaired fracture healing
Lidor et al ¹⁰	Implants of bone wax containing vitamin D in fractured chick tibiae	Decreased strength of the callus in the active group
Lindgren et al ¹¹	Rabbits	Impaired fracture healing in active group
Fu et al ¹²	Ovariectomized (“postmenopausal”) rats	A diet supplemented with vitamin D improved fracture healing
Delgado-Martinez et al ¹³	Elderly rats	Vitamin D improved fracture healing
Ömeroglu et al ¹⁴	Healthy guinea pigs	Vitamin D improved fracture healing
Ömeroglu et al ¹⁵	Healthy rabbits	Vitamin D improved fracture healing
Dekel et al ¹⁶	Chicks (initially depleted of vitamin D)	Vitamin D improved fracture healing
Brumbaugh et al ¹⁷	After fracturing the humerus, one group of chicks was deprived of vitamin D	These animals went on to develop rickets and showed prolonged fracture healing (ie, indirect evidence of the benefits of vitamin D for fracture healing)
Lindgren et al ¹⁸	Adult rats	Animals given vitamin D had a stronger fracture callus and slightly less pronounced postfracture osteopenia

(ie, articles on the benefits of vitamin D for fracture healing), 11 of these were in animals. In all, 2 animal studies showed neutral,^{8,9} 2 negative,^{10,11} and 7 positive¹²⁻¹⁸ results (see Table 1 for summary). Thus, the conclusions for clinical practice remain circumstantial at best.

There were only 2 human trials: 1 was a clinical case study examining whether patients with particular types of fracture nonunions had metabolic or endocrine abnormalities.¹⁹ The clinical relevance of this hypothesis is obvious. Most of the patients did indeed have such abnormalities, with vitamin D deficiency being the most common. But the results of the interventions (correcting metabolic or endocrine abnormalities) do not really speak for themselves: nearly three fourths of these patients still needed a surgical procedure for fracture healing.

There was only 1 randomized double-blind placebo-controlled trial in humans: Doetsch et al²⁰ recruited 30 elderly Danish women with a proximal humerus fracture, osteoporosis, or osteopenia (based on a hip scan), and not taking any medication related to bone formation. The participants either received placebo or vitamin D supplementation (ie, 800 U/d cholecalciferol and 1000 mg calcium). Standardized scans for bone mineral density (BMD) over the fracture area were similar at baseline but showed significantly higher BMD levels in the active group by week 6. They concluded that supplementation of vitamin D₃ and calcium had a positive influence on fracture healing in women with reduced bone mass.

Although this result might seem encouraging, the major weakness of this study is the low number of participants (n = 30).

The paucity of human studies begs the question, whether this is due to methodological difficulties and ethical hurdles encountered designing such studies, or due to the possibility that negative study results have been suppressed (publication bias).

So, what are we to conclude for clinical practice? As stated above, the typical elderly patient with a fracture is low on vitamin D, but most importantly, is at risk for further falls and fractures. Two large prospective cohort studies examined the incidence of a first (initial) fracture and the risk of subsequent fractures in elderly men and women.^{21,22} The result was “fractures beget fractures.” Of particular interest is the fact, that even “high-trauma” fractures (eg, sustained in motor vehicle accidents) should be considered “osteoporotic” in the elderly individuals.²²

In conclusion, a clear statement on the benefits of vitamin D for fracture healing awaits further trials, but all types of fractures in the elderly individuals indicate the need for secondary prevention and the implementation of appropriate guidelines concerning falls, vitamin D, and osteoporosis.^{3,4,21,23-26} A Swiss survey has shown that “osteoporosis remains underdiagnosed and undertreated in patients aged 50 years and older presenting with a fragility fracture.”²⁷ Meta-analyses indicate that vitamin D should always be given together with calcium,^{25,28} and one study demonstrated that large boluses of vitamin D are counterproductive.²⁹

The National Osteoporosis Guideline Group (NOGG) —to cite just one example—recommends a daily intake of at least 1000 mg of calcium, 800 U of vitamin D, and 1 g/kg body weight of protein as a general measure for osteoporosis prevention, see www.sheffield.ac.uk/NOGG for further details.²³

Conclusions

- A clear statement on the benefits of vitamin D supplementation for fracture healing awaits further trials. There is a huge gap in our knowledge on this topic in humans.

- All types of fractures in elderly individuals indicate the need for secondary prevention and the implementation of appropriate guidelines concerning falls, vitamin D, and osteoporosis, particularly as the typical elderly patient with a (hip) fracture has relevant vitamin D deficiency.
- Guidelines recommend a daily intake of at least 1000 mg of calcium, 800 U of vitamin D, and 1 g/kg body weight of protein as a general measure for osteoporosis prevention.

Declaration of Conflicting Interests

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