THE CONNECTION BETWEEN VITAMIN K & BONE HEALTH

Jamy Fu
Grade 11, Earl Haig Secondary School, Toronto District School Board (Toronto, Ontario), Mentor: Dr. Lora Giangregorio (University of Waterloo)

ABSTRACT

Vitamin K is essential to the body because it is known to help blood coagulate and activate osteocalcin, a protein involved in maintaining healthy bones. In this review, one study observing the impact of vitamin K supplementation on patients’ bone mineral densities and three studies focusing on the effects of vitamin K supplementation on the incidence of bone fractures are discussed to determine whether the vitamin may be important for maintaining bone health. While some promising results, such as an increase in bone mineral density of subjects after vitamin K supplementation arose, the conclusions reached by the four studies were not statistically significant enough to justify the importance of vitamin K in maintaining bone health. Well-controlled studies that are unbiased, statistically powerful, and focused on vitamin K’s effects on bone density are required in the future to provide further insight on whether vitamin K supplementation is a viable method of improving bone health.

INTRODUCTION

Vitamin K are a group of fat soluble compounds, and exist in the natural forms of phylloquinone (vitamin K1) and menaquinones-n (vitamin K2), that are obtained through consumption of fat-containing foods or plants. Vitamin K2 takes many forms expressed as menaquinones-n (MK-n) where n is the number of repeating 5-carbon units; the vitamin K humans consume ranges mainly from MK-4 to MK-10 (1, 2, 3). Generally, Vitamin K is known to help the blood coagulate and help stop bleeding(4). While dietary vitamin K deficiencies are uncommon (due to the fact that vitamin K can be easily obtained from green, leafy vegetables), doctors will prescribe vitamin K (2.5-25 mg orally or injected for teenagers and adults) if the patient experiences excessive bleeding (from their nose, gums, or wounds) or heavy menstrual bleeding due to vitamin K deficiency(4). Vitamin K deficiency has also been linked to patients with osteoporosis, which is a disease where bone tissue is lost (resulting in brittleness of the bones) due to the fact that bone deterioration is a symptom of vitamin K deficiency(5).

The potential mechanisms of vitamin K with respect to maintaining bone health.

Vitamin K activates vitamin K-dependent proteins such as osteocalcin, through a process known as posttranslational carboxylation, causing transformation of their glutamate residues (Glu) into a gamma-carboxyglutamate (Gla) structural residue(6). Thus, the now-activated the vitamin K-dependent proteins can contribute to hydroxyapatite crystal formation that make up bone structure, replacing old or damaged bone with new bone tissue (5). Furthermore, vitamin K is known to prevent calcification of vascular tissue and may even
participate in calcium bone integration and bodily regulation. Thus, it has been suggested that vitamin K supplementation could increase bone strength through the previously mentioned mechanisms. Observational studies done in 1984 with 10 years of follow-up involving 72,327 women aged 38-63 years old have demonstrated that lower vitamin K1 and K2 intake combined with high serum levels of undercarboxylated (inactivated) osteocalcin is associated with a higher risk of hip fractures (10).

**DISCUSSION**

*What do the research clinical trials say about vitamin K efficacy to bone health?*

Clinical trials conducted to evaluate the effect of vitamin K2 on fracture incidences and overall patients’ bone health produced inconclusive results. In 2012, Fang et al. conducted a meta-analysis in Anhui Medical University, China, observing 17 clinical trials that evaluated the effect of vitamin K on bone mineral density (or simply BMD) in patients eighteen years or older with osteoporosis (a disease where the incidences of bone fracturing is high due to bone mass decrease and tissue deterioration) (4). Each patient were either given vitamin K2 (in ten trials, eight of them were supplemented with MK-4 15-45 mg/day and two with MK-7 0.2-3.6 mg/day) or vitamin K1 (in seven trials 0.2-10 mg/day) supplements (6). After 6 to 36 months of vitamin K supplementation, no significant increase of BMDs was observed in patients’ femoral necks, but the average BMDs of the patient’s lumbar spines increased by 1.3% (6). Specifically, patients given vitamin K2 treatments experienced a significant 1.8% increase in their average lumbar spine BMDs, while patients treated with vitamin K1 supplements did not experience the same significant increases in their average BMDs (6). However, due to possible selection bias (where each patient may have had different baseline consumptions of vitamin K before the trials/treatment), detection bias (where diagnostic methods used to determine the increase in average BMD may be inconsistent to favour a higher increase in average BMD), and publication bias (exclusive presentation of trials with statistically significant BMD improvements) (6), the study failed to definitely determine whether vitamin K supplementation had significant effects on BMD in its sample population and patients.

Furthermore, a 2006 review and 2009 study report describe 8 clinical trials that assessed the effects of vitamin K2 supplementation on fracture incidence in osteoporotic Japanese patients (7, 8). Seven trials conducted in the 2006 study showed significant reduction in hip, vertebral, and nonvertebral fractures from adults supplemented with vitamin K2 (MK-4 of 15-45 mg/day) over 12-24 months (7). However, the 8th ‘outlier trial’ in 2009 demonstrated that vitamin K2 supplementation did not significantly reduce the incidence of fracturing. This trial included 4378 Japanese postmenopausal women aged 50 years or older with varying degrees of vertebral fractures that received vitamin K2 (MK-4 45 mg/day) and calcium supplements (oral calcium L-aspartate 1.2 g/day or dibasic calcium phosphate 3 g/day) for three years (plus a one year follow-up) (8). The results in the trial showed that simultaneous supplementation of vitamin K2 and calcium versus calcium alone did not significantly reduce the incidences of vertebral and all clinical fractures (all fracture that were reported and brought to medical attention), even after 3-4 years (8).

More recently, a 2013 Dutch study compared fracture incidence between an experimental group of 120 non-osteoporotic postmenopausal women that received vitamin K2 supplementation (with 0.36 mg/day of MK-7) and a control group (with 124 postmenopausal women) that received no supplementation (5). Unfortunately, the number of fractures was too low in both groups to definitely prove that vitamin K2 supplementation could decrease fracture incidence, since only one woman in the experimental group suffered a vertebral fracture compared to six women in the control group (5).

Lastly, one study done in Canada provided vitamin K1 supplements (5 mg/day) to 440 postmenopausal Canadian women with low BMDs between 2-4 years to observe vitamin K1 supplementation on bone health (10). The study involved a clinical trial where the control group was given a placebo and the experimental group received the vitamin K1 supplementation (the researchers or groups did not know which patients received the specific treatments). While the study reported significant results (9 women experienced 11 fractures in the experimental group, compared to the control group where 20 women received 21 fractures), the study
failed to conclude that vitamin K1 can decrease clinical fracture incidence because there are very few studies that investigate the relationship between vitamin K1 and clinical fractures and it is unknown whether more studies done in the future would support or reject the results of this study[9].

Therefore, the four studies discussed demonstrate that bone health in patients cannot be definitively improved with vitamin K2 or K1 supplements due to the inconsistent results and methodological limitations of the clinical trials presented in those studies. Thus, larger and better controlled clinical trials need to be conducted in the future to provide consistent data to definitely demonstrate that vitamin K supplementation has significant benefits on bone quality and health.

Research Gaps & Future Directions

Although the bodily presence of vitamin K can activate vitamin K-dependent proteins like osteocalcin to enhance its ability to bind to bone mineral[3, 5], the clinical trials described in this review demonstrate that vitamin K supplements may not significantly benefit bone health, whether through increasing BMDs or preventing incidences of bone fractures[2, 3]. To avoid this research gap, better controlled research is required to specifically understand how vitamin K consumption may prevent bone fractures or what conditions must be met for vitamin K to improve BMD significantly. For example, it is possible to hypothesize that vitamin K increases BMD more prominently in patients with osteoporosis because osteoporotic patients have a naturally lower BMD; osteoporosis could possibly be a condition that must be met for vitamin K to have a significant effect on BMD.

Ultimately, future research should involve statistically well-designed, controlled, and transparent studies that provide consistent treatments of vitamin K supplementation and maintain baseline vitamin K intake, focusing on the incidences of fractures and bone quality (i.e. BMD) as a primary outcome, specifically observing the effects of vitamin K1 consumption. If these criteria are met, then it may be possible to avoid inconsistencies that were encountered in previously mentioned clinical studies, decreasing the occurrence of selection, methodological, and publishing biases. Currently however, there is not enough statistically significant evidence to recommend vitamin K supplements as a method to improve bone health.

KEY WORDS Vitamin K; fractures; bone mineral density; bone health; phylloquinone; menaquinones; carboxylation; osteoporosis.

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REFERENCES
