Vitamin K2

Vitamin K2: Putting Calcium Where It Belongs

Vitamin K2 provides major protection from osteoporosis, cardiovascular blockages and pathological calcification.

Vitamin K's job is to put calcium in the right places and keep it from being deposited in the wrong places. The right places are bones and blood, and the wrong places include calcification of the vessels, bone spurs and calcification of soft tissues.

Vitamin K: Its Relationship to the Optimal Tissue Distribution and Function of Calcium

It has been shown that calcium has a ubiquitous role in health, impacting on essentially all the Syndrome X conditions and diseases, which include obesity, blood pressure disorders, cardiovascular disease, diabetes, and malfunctioning of cell signaling. Calcification of the arteries is a major known consequence of aging, as is the calcification of soft tissues and the accumulation of calcium intracellularly (within the cells).

Optimum calcium nutrition depends on the interplay of a number of related compounds, such as magnesium, vitamin D3, and vitamin K. Just recently, the importance of vitamin K in regulating the healthy function of calcium has been recognized. It has been shown that vitamin K2 can be supplemented in very high doses, as used in Japan. It has been found to be safe even at 45 mg or more per day - up to a thousand times greater than generally occurring in the daily diet. Even small amounts of vitamins K1 & K2, as we will see, can have a great impact on overall health.

Vitamin K1 and more importantly, vitamin K2, play critical roles in preventing arterial calcification, which is a risk factor in coronary artery disease, as well as other calcification conditions associated with aging.

Vitamin K is actually a group name for related compounds, which all have a similar molecular structure (methylated naphthoquinone ring structure).

Vitamin K was discovered in the 1920's as a fat-soluble factor important in blood coagulation ("K" for koagulation). Vitamin K1 is found in plants and vitamin K2 is found in animals and bacteria, including beneficial probiotic bacteria, aka "good bacteria," from the GI tract. The body can store about a one-month supply of the vitamin. Antibiotics interfere with the growth of healthy intestinal bacteria and as a result, impair vitamin K production. The prescription anticoagulant Warfarin also interferes with the metabolism and function of vitamin K by inhibiting critical enzymes that are involved with the production of coagulation factors. Without these coagulation factors, excessive bleeding can occur.

How this vitamin is involved in blood coagulation eluded scientists until 1974, when a requirement for vitamin K was shown for the formation of numerous proteins in the body

known as gamma-carboxy glutamic acid (GCGA) proteins. These proteins, when modified, specifically bind to calcium which is important for blood coagulation, as well as other critical processes, and through which calcium regulation affects cartilage, bone, protein in blood, and very importantly, regulates the calcium in the cardiovascular system. It appears that the extra carboxyl group binds calcium so that it can be moved around.

What Are GCGA Proteins?

Vitamin K works by acting as a cofactor in the carboxylation (adding of a carboxyl group C02) via an enzyme (gamma glutamyl carboxylase), of glutamic acid (a specific amino acid) to form a modification of that amino acid (gamma carboxyglutamic acid) in a variety of critical plasma proteins. Without this step, these plasma proteins will not function in their role of the regulation of calcium concentrations in various tissues.

There are several different types of GCGA proteins including: osteocalcin (OC), which is the most abundant GCGA protein in humans and is synthesized in bone; the GCGA protein containing blood coagulation factors are synthesized in the liver; the matrix GCGA proteins (MGP) are synthesized in the cartilage and in the vessel walls of arteries. 1

According to the Food and Nutrition Board of the National Academy of Sciences National Research Council, the requirements of vitamin K in micrograms (mcg) ranges from 5 micrograms for infants and up to 80 mcg for adult males and 65 mcg for adult females. 2

When vitamin K is in short supply in the body, these proteins are formed without the GCGA component and are inactive for their intended functions - which play important roles in four different tissue types including: 1) liver; 2) bone; 3) cartilage; and 4) arterial vessel walls.

These four tissues are all able to pull vitamin K from the blood. However, the uptake from the liver is much greater for K1 than for other tissues. Very important recent findings indicate that vitamin K2, and not K1 inhibits Warfarin-induced arterial calcification. This research is important for those on Warfarin, and has implications for the majority of us who are unaware that we are deficient in this lifesaving nutrient.

Because the liver needs so much vitamin K, this can leave the cartilage and bone GCGA proteins with inadequate levels. Hence the dietary vitamin K requirement for bone, and the special requirements for the cardiovascular system and cartilage may not be met even though normal clotting factor production occurs, as this occurs in the liver. Therefore, the requirement to keep the vasculature clear of accumulating calcium and to keep the bones well supplied with calcium may not be adequately supplied. This is why the recent discoveries on the value of vitamin K2 and its recent commercial availability can make a great difference in the lives of millions - probably a majority of the population would benefit.

The FDA's current recommendations for vitamin K dosage is based solely on the liver's requirements alone. It has been identified that a large percentage of the enzymes that do not receive GCGA because of a vitamin K1 or K2 deficiency, become unable to mobilize calcium and place it into the bone where it belongs. This GCGA-deficient enzyme is known as under-carboxylated osteocalcin (ucOC). It was found that this occurs in the majority of the healthy

adult population indicating subclinical vitamin deficiency in a large portion of the population. 3,4 Though this is subclinical in terms of obvious symptoms, the first symptoms may be osteoporosis or acute coronary disease... the first symptom may even be death.

The results of a vitamin K intervention study have been examined in which both bone mineral density and vascular elasticity were shown to increase. 5 Other studies have demonstrated consistent findings adding to the conclusion that vitamin K1, and preferably, a good amount of vitamin K2, may be some of the best protection for preventing calcification of the arteries, and for protection against osteoporosis.

Oral anticoagulant medications such as Warfarin or Coumadin, etc., which are the most commonly used anticoagulants, are vitamin K antagonists. Vitamin K may lessen the concentration of the anticoagulants.

Scientific Studies

An excellent history and review of Vitamin K is offered in a number of scientific papers - one being Vitamin K1 supplementation retards bone loss in postmenopausal women between 50 and 60 years of age by Braam, Knapen, Geusens, Brouns, Hamulyak, Gerichhausen, and Vermeer, epub 2003. See below for more study results:

In 1984 it was found that patients with osteoporotic fractures had circulating vitamin K levels which were over 70% lower than those in the control group. 6 The data was consistent with other studies show ing that low serum vitamin K is associated with low mineral density, which is a high risk factor for bone fracture. 7-9

In analyzing British and American populations, it was found that they did not meet the RDA levels of 1.5 micrograms per day per kg of body weight (10-12) and that low intake is associated with low bone mineral density which is associated with risk of bone fracture.

In the Nurses Health Study, over 72,000 women between 38 and 63 years of age were followed for 10 years. The risk of fracture in the lower quintile for vitamin K intake almost doubled that in the higher quintile. 13

In the Framingham study of an older group of patients, with an average age of 75 years, the results were more dramatic. 14 Subjects in the highest quartile for vitamin K intake had a significantly lower hip fracture risk. 15

Hence the critical involvement of vitamin K in bone health and its general deficiency in our population is firmly established.

Vitamin K Supplementation Retards Postmenopausal Bone Loss

In the Maastricht osteo study, 188 postmenopausal women between 50 and 60 years old were treated for 3 years with daily supplements. 16 There was a placebo group which received only maltodextrin and the second group received minerals, 500 mg/day of calcium, 150 mg/day of magnesium, 10 mg/day of zinc and 320 IU/day of vitamin D3. The third group received these minerals plus the vitamin D3 and l mg/day of vitamin K1. The group without vitamin K benefited only transiently. In the group with vitamin K, bone loss at the femoral

neck was retarded by 35%-40% compared to the other mineral vitamin D group. It is stated that if these effects continued over decades, lifelong supplementation could postpone fractures by up to 10 years.

Further research of the D-Bavis study using calcium (1000 mg), vitamin D (10 ug) and vitamin K (200 mcg) per day, supported the previous findings. They also found a significant increase in bone mineral content and density in the vitamin K group. 17

The authors concluded that combined supplementation with vitamin K1 and D3 at dietary relevant levels improved bone mass density at the trabecular bone site and that the equivalent supplementation in high osteoporotic risk groups may be beneficial. Extremely high doses 45-90 mg/day of vitamin K2 are successfully used in the treatment of osteoporosis in Japan. 18-20 These doses of K2 exceed RDA levels by 1000 fold and no side effects were noted.

Low Vitamin K Intake as a Risk Factor for Cardiovascular Disease

256 postmenopausal women were studied by Jie, et. al. in the EPOZ study. They found an inverse correlation between long term vitamin K intake and arterosclerotic aorta calcification. 21 Only vitamin K1 (phylloquinone) was included in the study.

A subsequent study of 4500 participants of the Rotterdam study by Gelejinse, et. al. reports a much stronger negative correlation between long term, lower than adequate intake of vitamin K2 (menaquinone) and aortic calcification. The data was stronger for K2 than for K1. This is consistent with the suggestion of preferential uptake of K2 by the vessel wall. 22

Vitamin K Supplementation Prevents Age Related Vascular Stiffening

In an animal study in rabbits with high cholesterol, vitamin K2 was shown to decrease circulating cholesterol concentrations, suppress progression of vascular plaque, thickening in the vessels, and pulmonary atherosclerosis. 23 In a study of rats on arterial calcification, vitamin K2 completely prevented calcification, whereas vitamin K1 had little effect. 24 A three year study involving postmenopausal women (a group which is generally known to be at risk for vascular illness), the elastic properties of the carotid artery were recorded using ultrasound. A supplement of 1 mg/day of vitamin K1 completely abolished age-related arterial stiffening, whereas the placebo group showed a decrease of 13% of elastic properties of the vasculature during the test period. 25

Dietary & Supplemental Forms of Vitamin K1 & K2

Most of our dietary vitamin K1 comes from vegetables - about 80%. Vitamin K2 is obtained mainly from the "good" bacteria produced in the digestive tract and is also found in certain fermented foods. 26 The absorbability of the vitamin K2 from the GI tract bacteria is uncertain. 27 The absorption of vitamin K1 from vegetables is about 10%.

"However, both K1 and K2 are well absorbed from supplements as long as they are taken with some dietary fat to stimulate bile secretion." 28

Recommendations of a European Expert Group

In November 2002, a number of European experts in the fields of vitamin K research, bone metabolism and cardiovascular disease met to review all the available scientific data to formulate an opinion on the amount of recommended dietary vitamin K and the use of vitamin K-containing supplements, for optimal bone and vascular health. Some of the conclusions from this meeting are summarized below:

Daily intake of between 200 and 500 mcg/day of vitamin K through food sources may be required for optimal health.

Accumulating evidence suggests there is a synergistic effect between vitamins K, D and calcium (and of course, magnesium). Optimal health effects may be obtained from combined supplementation of vitamins K, D and minerals.

Any risks associated with high consumption of either vitamin K1 or K2 appear minimal, with intakes up to 1 mg/day of vitamin K1 and 45 mg/day of vitamin K2, often having been used with no observed side effects.

The only potential problem with high levels of vitamin K supplementation relates to interference with oral anticoagulant medications such as Warfarin and Coumadin, which are antagonists of vitamin K. Patients on oral anticoagulant treatment should not use vitamin K supplements and avoid strong fluctuations in their daily dietary vitamin K intake. However, in a systematic dose-response study of patients on oral anticoagulant therapy, it was demonstrated that the stability of anticoagulation was not significantly affected by vitamin K supplementation at doses below 150 mcg/day. 30 Patients on anticoagulant medications should consult with their physician or healthcare practitioner regarding vitamin K.

Other Benefits of Vitamin K

We have discussed the beneficial effects of vitamin K on bone density, cardiovascular health, and the Syndrome X diseases, however, there are even more benefits to vitamin K supplementation.

Anti-Inflammatory

Further research has demonstrated vitamin K's anti-inflammatory action. As the body ages, levels of the inflammation-promoting cytokine interleukin-6 (IL-6) increase. Once IL-6 becomes out of ba lance with the other cytokines, inflammation accelerates. It has been observed that people with arthritis, Alzheimer's disease, and atherosclerosis have higher levels of IL-6. In a study done by the National Research Institute in Italy, it was shown that subjects with the highest levels of IL-6 were almost twice as likely to develop mobility-related disabilities.

Diabetes

The second highest concentration of vitamin K in the body is in the pancreas, which plays a major role in blood sugar and insulin regulation. In animal studies, Japanese researchers found that when they induced vitamin K deficiency, the test animals developed Type II diabetes. 31

Antioxidant

Research has indicated that vitamin K has antioxidant activity comparable to vitamin E and CoQ10. 32,33 Animal studies have demonstrated complete hepatic (liver) protection from induced oxida tive stress using vitamin K, and was found to be 80% as effective as vitamin E in preventing oxidation.

Alzheimer's

About 25% of the population have a genetic predisposition for developing Alzheimer's disease - they carry the E4 form of the lipoprotein apoE. Interestingly, people who carry this gene have been found to have low levels of vitamin K. Calcification and the development of lesions in blood vessels that feed the brain tissues are believed to be a component of Alzheimer's development. Further research may reveal high-dose vitamin K therapy to be preventive.

Japanese Study on Vitamin K2 & Viral Cirrhosis-Related Liver Cancer

Japanese researchers have recently discovered that vitamin K2 may play a significant role in prevention of liver cancer caused by viral cirrhosis. In a 2004 study published in the Journal of the American Medical Association, 40 women diagnosed with viral liver cirrhosis were studied, in which 21 were given 45 mg vitamin K2 per day. Vitamin K2 was found to decrease the risk of the development of liver cancer in female patients with viral cirrhosis, possibly by delaying the onset of the cancer. 34 For over seven years, the patient's progress was closely followed. The proportion of patients who developed liver cancer was significantly smaller in the group of women treated with the vitamin K2 (2 of 21), compared to the non-treated group (9 of 19). The annual incidence of liver cancer in the treated group was 1.6%, compared to the non-treated group, which was 8.8%. The researchers believe that a substance called geranyl-geraniol (a by-product of vitamin K2), induces cell death in tumor cells suggesting that it may play an important role in cell growth inhibition. The researchers wrote, "The study indicates that vitamin K2 decreases the risk of liver cancer to about 20% compared to the control group." The researchers also commented that these are only preliminary results and further research needs to be done through clinical trials.

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