

Osteoporosis 2: The Vitamin K2 Story

Readers Summary

1. How does the human body handle vitamin K2?
2. Is the gallbladder important in the vitamin K2 cycle?
3. Why does osteoporosis walk hand and hand with arterial disease?
4. How is vitamin K2 linked to our lipid profile clinically?
5. How does coumadin cause iatrogenic osteoporosis?

In the first blog on osteoporosis, we focused in on how to stimulate bone mass accrual via our diet. This is by far the best way to fight osteoporosis and least used way, but it is not the only way to treat it. Eating a diet that is plentiful in proteins and saturated fats are smart moves to stave off bone loss as one ages. Eating a diet laden in carbohydrates or filled with a lot of fowl like turkey and chicken is not going to help your bone mass in the long run. The last blog demonstrated that vitamin K2 supplementation (for just 4 weeks) will not only increase your insulin sensitivity, but raise your sex steroid hormones as well to support your bone metabolism. Both mechanisms seem to be related to increased amounts of serum carboxylated osteocalcin (cOC), is made rather than just modulating inflammation in our body. The study I mentioned in part one, had too small a sample size to make firm interpretation on β -cell function result for a population, but the implications are huge for T2D with bad bone, bad heart or bad teeth. It is clear that vitamin K2 is biochemically quite helpful to a T2D with bone loss. The results of this study are consistent with previous studies found in the literature that demonstrated improved insulin resistance by treatment with vitamin K1 or vitamin K2, respectively. The preponderance of the research to date, is

pointing out to us that cOC rather than uncarboxylated OC, is the endocrine hormone that increases insulin sensitivity in humans and eventually leads to increased bone mass. It appears the underlying mechanism for this uses inflammatory cytokines and involves leptin receptor dysfunction. It appears that cOC and/or vitamin K2 likely modulates several adipokines and inflammatory pathways other than the classic IL-6 pathways to offset bone loss seen in leptin receptor disease states. Since Vitamin K2 is a critical component of arterial, gut, and bone health, we need to spend some time talking about how the human body handles vitamin K2 in part two of this series. Vitamin K2 up regulates testosterone and it helps both sexes remain somewhat hydrated. This will become important when we hit quantum biology in the blog.

Vitamin K recycling and GB: The HDL Link to the leaky gut

The body, in its Optimal state, is very efficient at utilizing vitamin K by recycling it. It uses a process called “cyclic interconversion” to regenerate the vitamin K in the body. In this cycle, the vitamin K in the quinone form is reduced by the FAD-containing enzyme DT-diaphorase (called NAD(P)H quinone oxidoreductase) into the vitamin K hydro-quinone (KH₂). The KH₂ serves as the direct cofactor for vitamin K’s carboxylation of the Gla-protein. By undergoing this step, it allows KH₂ to be oxidized to a vitamin K epoxide. Vitamin K epoxide is then recycled back to the original quinone form mentioned earlier by the enzyme vitamin K epoxide reductase (VKOR), completing the cycle. The VKOR enzyme is the enzyme that is blocked by warfarin or coumadin type anticoagulants. The gene for VKOR has recently been identified, and it appears that most of the clinical variability observed in patients’ response to warfarin is attributable to variability in the human VKOR gene. This is why so many people have wide range responses to these drugs on their INR blood testing. Coumadin

works by blocking all vitamin K dependent clotting factors and this thins one's blood to clotting. On a bio-molecular level, vitamin K epoxide is reduced in two steps: first to the quinone form by VKOR, then to vitamin K hydroquinone (KH₂) by a DT-diaphorase. The KH₂ form is a big player in arterial and cardiac valve health.

The arterial and cardiac issues with K₂

KH₂ also possesses a major antioxidant action in arteries, and is highly sensitive to free radicals in those tissues. KH₂ is so reactive, that it may oxidize (and inactivate) further KH₂ production before it can take part in the carboxylation reaction in which it serves as a cofactor. This heightened reactivity of KH₂ to free radicals may increase our dietary needs for vitamin K₂ in arterial walls inflicted with an atherosclerotic plaque to protect them from PAD. In these plaques, we find high levels of oxidized LDL. The oxLDL came from LDL cholesterol made in the liver that spent too much time circulating in oxidized plasma. The main reason for this is poor endocytosis in the portal circulation and/or poor LDL receptor function causing it not to be uptaken quickly enough by the cells of our body. When this occurs, we generally also find in serum assays a particle size change to sdLDL and a lowered HDL level. It also appears the action of the CETP enzyme is disordered. We also find that patients are often leptin resistant at the liver level and tend to have lower sex steroid hormone levels and increased SHBG. Vitamin D and pregnenolone levels are also diminished clinically on blood testing as well. The more oxidized the LDL becomes, the more oxLDL finds its way into an atherosclerotic plaque and depletes body stores of Vitamin K₂. This contributes to a local vitamin K deficiency because of the extreme reactivity of KH₂ form of Vitamin K₂ to the oxLDL. This process becomes a vicious cycle and further exacerbates the atherosclerotic

process in the arterial wall. This is why many studies, like the Framingham Study, have shown extreme low levels of vitamin K in diseased arterial walls and heart valves leading to disease and eventually an earlier death.

For every increase of **10 micrograms** in the amount of vitamin K2 consumed daily, the risk of developing coronary heart disease (CHD) drops by **9 percent**. This statistic was noted as a result of a cohort study from the Netherlands evaluating the dietary vitamin K intakes of 16,057 post-menopausal women and their association with the incidence of CHD. Many people/doctors seem unaware of this data. When I see a low Vitamin D levels I usually tell the person with bad bones, a bad heart or bad teeth to increase their vitamin K2 200mcgs for every 1000 IU of D 3 they are supplementing. This is the magic that helps them “begin” to rehydrate.

- <http://www.ncbi.nlm.nih.gov/pubmed/19179058>
- <http://www.ncbi.nlm.nih.gov/pubmed/11180916>

VKOR is critical to the human K2 recycle

The VKOR is the crucial enzyme in vitamin K metabolism in humans. It enables Vitamin K's recycling after it has been oxidized in the carboxylase reaction through which it activates Gla-proteins. KH2 is a cofactor in this crucial step. Vitamin K2 carboxylates the Gla-proteins of osteocalcin to stimulate osteoblasts to make new bone and prevent osteoporosis. Because of the VKOR recycling, the human dietary requirement for vitamin K is extremely low. It is just 45 mcg/day when things are working optimally. Of course if the gut is not working well for any reason, the dietary needs can skyrocket. The gut microbiome can make vitamin K, provided there is a normal gut flora state. From the gut microflora, the vitamin K concentrates in the liver for storage until it is needed. Storage is small, because Vitamin K2 is used

rapidly in the human system. Vitamin K2 is absorbed from the jejunum and ileum. As with other fat-soluble vitamins, absorption depends on the presence of bile and pancreatic juices, and is enhanced by dietary fat. If one does not have a gallbladder, this can present a problem in absorption of K2. Although the liver is the main storage site, vitamin K2 is also found in some extrahepatic tissues, like bone and the heart. The cardiac valves are a rich source of Vitamin K2 in normal humans. Liver stores consist of about 10% phylloquinones and 90% menaquinones. Compared with that of other fat-soluble vitamins, the total body pool of vitamin K is very small and turnover of vitamin K in the liver is rapid. This turnover increases greatly when the plasma is chronically in the oxidized state. This is very common when one eats a SAD, has arterial disease or has osteoporosis. Vitamin K2 is secreted from the liver into the hepato-biliary tree (GallBladder) and then released into gut. During its sojourn in the portal and general circulation, its job is to protect our arteries and heart from developing peripheral artery disease (PAD) or calcific valvular disease. It also prevents osteoporosis in the skeleton too. If one has a lot of PAD and/or metabolic bone disease, little of the Vitamin K2 comes back to the liver for storage and reuse. The K2 that does return is then reabsorbed by the liver and concentrated and secreted in our bile acid back into the GI tract. Then it is recycled once again throughout our plasma and back to our liver. If one has a cholecystectomy, (gallbladder removed) this results in a loss of efficiency of the Vitamin K2 recycling. When this occurs, the only way to replace it is via dietary sources which are notoriously sparse in the Western diet. Thus, in cases where the GI tract has dysbiosis or gallbladder disease (missing GB!) one might consider supplementing Vitamin K2 to offset the efficiency losses of the Vitamin K2 recycling in the body. If you do, you might want to also consider a bile

acid replacement to absorb it as well.

The liver contains 90% of the menaquinones synthesized by gut bacteria, but no one seems to know the precise rate of absorption of the menaquinones in human altered states as yet. This makes estimating their contribution to the human vitamin K requirement a question mark even today. A clinician, however, can make a good guesstimate of the needs by knowing how Vitamin K is recycled and assessing a patient's labs and reviewing their medical history. Once the clinician realizes the importance of this recycling system, they can estimate the K2 losses by looking at the HDL levels and sdLDL levels in the lipid profiles of patients. I also screen the HS CRP and Vitamin D levels as well to get a clearer idea of what the losses might be in total. The reason for this is that both of these tests give us insight into how oxidized the plasma currently is. The more oxidized it appears, the higher the vitamin K2 losses will likely be. In cases where HDL is quite low, thus signifying a highly oxidized plasma, I usually will recommend Vitamin K2 replacement. If the HDL levels are low and this is confounded by low sex steroid hormones, gallbladder disease, low vitamin D levels, and an elevated HS CRP I generally recommend a higher dose of Vitamin K2 twice a day to offset recycling losses. In dysbiosis cases (IBD), this ability is often severely altered and dietary and supplement replacement becomes a more dire need for both bone and arterial protection. If osteoporosis is present, I use very high doses of vitamin K2 to treat it.

Are PAD and osteoporosis bed fellows?

Yes they are. Why? Most patients with vascular claudication are found to have calcified arteries and high calcium index

scores. They also tend to have calcified vessels on regular screening x-rays we use in spine disease work ups. This is precisely how I find most cases of undiagnosed osteoporosis in my clinic. It appears medicine has forgotten about the link between dystrophic calcification in arteries and bone due to vitamin K2 depletion. This clinical situation becomes even more serious if the patients' plasma is more oxidized, resulting in a poor lipid profile on the VAP or NMR testing. This is also why I will order a VAP or NMR on osteoporotic patients. Since VKOR is the target for warfarin and coumarin related derivatives, when it is given chronically by cardiologists or vascular surgeon for heart disease or for PAD, it causes severe bone loss and severe arterial calcifications. This is due to blocking the recycling of vitamin K2 by inhibiting VKOR. Thus, it decreases vitamin K2 that remains available for the activation of Gla-proteins on carboxylated osteocalcin. So long term coumadin use is a problem for the skeleton. The longer it is used, the more severe the metabolic bone loss becomes. This cause of osteoporosis is today very common because PAD is a very common disorder in those eating a SAD. I refer to this disease as "iatrogenic osteoporosis". When this occurs, and a patient still requires anticoagulation, we have the ability to request of the cardiologist or the vascular surgeon to stop the use of Coumadin, and go to other non Vitamin K clotting factor blockers when the patient has co morbid metabolic bone disease. The Vitamin K dependent clotting factors are Prothrombin (factor II), factors VII, IX, and X, and proteins C, S and Z ,are proteins that are involved in the regulation of blood coagulation. They are all synthesized in the liver. Some other drugs that can be used in this case are non Vitamin K dependent blood thinners like, Pradaxa and a combo of Lovenox and aspirin. There are also several other new anticoagulants in final trials due to be released in the next year or so. Help is on the way for patients who have PAD, calcific heart valve disease, and metabolic bone disease. PAD and osteoporosis are diseases of dehydration.

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Cites

- Yadav VK, Ryu JH, Suda N, et al. Lrp5 controls bone formation by inhibiting serotonin synthesis in the duodenum. Cell 2008;135: 825-837.
- GASTROENTEROLOGY 2011;141:439-442
- <http://care.diabetesjournals.org/content/34/9/e147.full>

- Shea MK, Booth SL, Gundberg CM, Peterson JW, Waddell C, Dawson-Hughes B, Saltzman E: Adulthood obesity is positively associated with adipose tissue concentrations of vitamin K and inversely associated with circulating indicators of vitamin K status in men and women.
- J Nutr. 2010 May;140(5):1029-34
- PMID: 17145139 [PubMed – indexed for MEDLINE]
- Wu S, Liao AP, Xia Y, Li YC, Li JD, Sartor RB, Sun J: Vitamin D Receptor Negatively Regulates Bacterial-Stimulated NF- κ B Activity in Intestine. Am J Pathol. 2010 Jun 21
- <http://www.ncbi.nlm.nih.gov/pubmed/16942519>