New Research in Vitamin D and Cardiovascular Disease: Expanding Our Approach Beyond Lipids and Blood Pressure

In 2008 alone, there has been a steady stream of published studies on the influence of vitamin D deficiency in cardiovascular disease, peripheral artery disease, blood pressure, endothelial function and cardiovascular mortality. If we didn’t have enough reasons already to increase our awareness of vitamin D insufficiency and deficiency, here is more motivation.

Vitamin D Deficiency and Increased Risk of Cardiovascular Disease

1,739 offspring (Caucasian) of the original Framingham Heart Study were eligible for the Framingham Offspring Cohort. Mean age was 59 years; 55% were women (947) without prior cardiovascular disease. 25-hydroxyvitamin D levels were measured, and deficiency groups were identified as < 15 ng/mL and < 10 ng/mL. 28% of individuals had levels < 15 ng/mL and 9% had levels < 10 ng/mL. With an average follow-up of 5.4 years, 120 participants developed a first cardiovascular event. Those with a serum vitamin D level < 15 ng/mL had a hazard ratio of 1.62 for cardiovascular events compared with those with a 25-OH level ≥ 15 ng/mL. This effect was observed in those with hypertension but not those without. There was a progressive increase in cardiovascular risk with lower levels of vitamin D with a 1.53 hazard ratio for levels 10 to < 15 ng/mL and 1.80 for levels < 10 ng/mL.

The results of this study suggest that moderate to severe vitamin D deficiency is a risk factor for developing cardiovascular disease. One would hope that treatment of vitamin D deficiency with supplementation or adequate exposure to sunlight could reduce that risk. While a randomized intervention trial would be needed to assess vitamin D supplementation as a treatment strategy, we do have other positive evidence showing vitamin D supplementation reducing blood pressure, ventricular hypertrophy, and inflammatory cytokines.

Vitamin D and Hypertension

Serum vitamin D concentrations were evaluated to determine if there was any relationship to systolic blood pressure (SBP) in the third National Health and Nutrition Examination Survey (1988–1992). Blood pressure was classified with six categories. A statistically significant inverse association was observed between circulating 25(OH)D concentrations and SBP ranging from normotensive to mildly hypertensive in white participants. 25(OH)D concentrations > 80 nmol/L decreased the age-related increase in SBP by 20% as compared with those having < 50 nmol/L. Due to decreases in vitamin D production in older adults, the decreased 25(OH)D concentrations associated with increasing age overwhelmed the association of 25(OH)D with SBP in this study. However, those participants in this study who were vitamin D deficient had the strongest association of aged with SBP, and those > 65 had the strongest association. Those with 25(OH)D concentration < 37.5 nmol/L were at increased risk of hypertension.

Two earlier randomized clinical trials support the role of vitamin D in reducing blood pressure.

A note about testing and treating vitamin D deficiency: Make sure to note and be clear as to your units and reference ranges for nmol/L vs. ng/mL.

Serum Vitamin D and Peripheral Arterial Disease

Data from 4,839 participants in the National Health and Nutrition Examination Survey 2001 to 2004 was analyzed to evaluate the relationship between 25 (OH)D and peripheral arterial disease (PAD). Participants were characterized by PAD status, and the prevalence of PAD was calculated by quartile of 25 (OH)D. There was a strong graded association between lower 25 (OH)D levels and a higher prevalence of PAD. The prevalence of PAD was 1.80 for those with a serum D < 17.8 ng/mL and 1.19 for those with a level ≥ 29.2.

In the analyses of multiple subgroups, the association appeared stronger for non-Hispanic whites and for those without diabetes mellitus. Although a limitation of this study is that it was cross-sectional, it is similar to two previous smaller studies of 25 (OH)D and PAD. Given that approximately 5 million US adults are affected by PAD and its association with a high risk of morbidity and mortality from cardiovascular disease, assessment of serum 25 (OH)D levels is a simple test to reduce this risk.
This would be especially useful in those with risk factors for PAD – including dyslipidemia, diabetes mellitus, hypertension, smoking, and inadequate kidney function.

Improving Endothelial Function in Type 2 Diabetics with Vitamin D Supplementation

A double-blind, placebo-controlled randomized trial was conducted to test whether a single large dose of vitamin D2 could improve endothelial function in type 2 diabetics with a low serum 25(OH)D level. Participants were included if their winter baseline of 25 (OH)D was < 50 nmol/L. A single dose of 100,000 IU vitamin D2 or placebo was administered during the winter months. Vitamin D supplementation increased serum levels by 15.3 nmol/L relative to the placebo, and improved flow mediated vasodilatation by 2.3%, after adjusting for blood pressure changes. Supplementation also decreased systolic blood pressure by 14 mm Hg. Given that endothelial function is an important predictor of cardiovascular events, this simple intervention in diabetics with low vitamin D levels and a high risk of cardiovascular disease provides a safe, inexpensive approach to reducing cardiovascular events. My habit for those with a vitamin D insufficiency (< 50 nmol/L or 30 ng/mL) or deficiency (< 20 ng/mL) is to dose 100,000 IU of vitamin D2 once per week for two months and then retest. A maintenance dose would then have to be determined.

It’s Not All About Treating Hyperlipidemia and Hypertension

One of the most eye-opening experiences I’ve had in relationship to cardiovascular disease was hearing a lecture and reading an article by John Abramson, MD. In an interview published in Townsend Letter (June 2008), he stated: “There is not a single randomized controlled trial that shows that cholesterol-lowering statin drugs are beneficial for women of any age or men over 65 who do not already have heart disease or diabetes.” He also stated that even the 2001 National Cholesterol Education Program guidelines admit that clinical evidence for its recommendations regarding statins for women was generally lacking and it was based on extrapolation of the data from men. He also asserts that there’s no evidence that statins reduce cardiovascular events for men or women over age 65 who do not have heart disease or diabetes.

If you’ve not already been alarmed by the push for statins as primary heart disease prevention, you will want to know that in 2006, 1.3 million coronary angioplasty procedures were done in the US at a cost of $48,399, and 448,000
coronary bypass operations at a cost of $99,743. That’s a total of over $104 billion. For those two procedures alone, we spent more than $100 billion in 2006. If these procedures accomplished as much as they cost, that would be one thing, but even the New England Journal of Medicine reported in 2007 that angioplasties and stents do not prolong life or prevent heart attacks in stable patients; stable patients are 95% of those who undergo those procedures. And...sadly, coronary bypass surgery prolongs life in less than 3% of patients.

We have good scientific evidence that diet and lifestyle changes can prevent at least 90% of all heart disease. 90%! In yet another recent study proving this point, an intervention diet (either low-fat or Mediterranean) significantly improved cardiovascular-event-free survival in those who had previously had a heart attack. The well-known Lyon Diet Heart Study also demonstrated a survival advantage with the Mediterranean diet.

For both primary and secondary heart disease prevention, we have to step up our efforts in helping our patients “get religion” about rigorously changing their eating habits, losing weight, exercising a minimum of 30 minutes every day (and for overweight women 40 and over, likely 60-plus minutes daily), and, of course, stopping smoking.

In addition to using nutritional and botanical supplementation to address any lipid or hypertension issues, a diverse approach attending to arterial health and inflammation deserves our attention as well. While questioning statins, we might also want to question our own use of nutraceuticals in treating hyperlipidemia with items such as soluble fibers, soy, red yeast rice, niacin, phytosterols, pantethine, tocotrienols, resveratrol, policosanol, gugulipids, or garlic. I have as of yet not abandoned this thinking of improving lipid profiles, but a broader perspective is in order. While of course attending to normalizing blood pressure (magnesium, potassium, bonito protein, marine omega-3 fatty acids, vitamin D, lycopene, Pycnogenol, hawthorn, L-arginine, carnitine, NAC, and more), I have also expanded my attention to arterial health with attention to dilatation, anti-inflammation, reduction of LDL oxidation, platelet function, and reducing vascular calcification.

I look more to combination ingredients and product formulations that approach cardiovascular health from the multimechanism perspective. While not an exhaustive list, here are items to consider beyond lipid therapies:

- **Dilatation:** L-arginine, quercetin/flavonoids, vitamins C and E, magnesium, coenzyme Q10, taurine, garlic, soy;
- **Anti-inflammation:** marine omega-3 fatty acids, flax oil, isoquercetin, quercetin/rutin/flavonoids, resveratrol;
- **Reducing LDL oxidation:** niacin, green tea, garlic, pantethine, resveratrol, policosanol, coenzyme Q10;
- **Anti-thrombosis:** marine omega-3 fatty acids, garlic, pomegranate, nattokinase, ginger, resveratrol;
- **Reducing vascular calcification:** vitamin K2, marine omega-3 fatty acids.

More than 500,000 women die of cardiovascular-related causes annually in the US, approximately 100,000 prematurely, before age 65. Starting at age 50, more women die of cardiovascular diseases than of any other condition, and women younger than 55 who have a heart attack have a worse prognosis and higher incidence of related death than do men of the same age who have a heart attack, as well as a greater chance of having another heart attack. Disability due to cardiovascular disease is also a major concern, especially in older women. And for African-American women, the risk of heart-related death is even greater – twice as high as for Caucasian women.

To be successful in our mission of preventing and treating heart disease, and helping our patients with the difficult challenges of weight loss and lifestyle changes, we must enhance patient education, expand our strategies for motivation, improve and broaden our prescribing of plant- or nutrient-based supplements, and continue our wise and considered use of pharmaceutical/conventional interventions.

Notes