Vitamin D Intake Lowers IL-6 Levels in the Context of Weight Loss

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Overweight or obesity is associated with an increase in chronic inflammation, which in turn is associated with increased risk for several diseases, including various cancers. Several studies have suggested that vitamin D deficiency may be associated with increased inflammation levels. Being deficient in vitamin D also appears to be associated with higher levels of circulating inflammatory markers. While weight loss is associated with reductions in inflammatory biomarkers, it is not known whether vitamin D supplementation might further boost this effect. To evaluate this question, Drs. Catherine Duggan, Anne McTiernan, and colleagues in the Public Health Sciences Division evaluated data from a recent randomized clinical trial of vitamin D3 supplementation vs. placebo in the context of weight loss. Reporting their results in *Cancer Prevention Research*, the authors found that vitamin D3 supplementation lowered IL-6 levels compared to placebo, but only among those who lost at least 5% of their baseline weight.

Vitamin D is a steroid hormone that plays a significant role in calcium homeostasis and metabolism. Humans obtain vitamin D primarily through dermal synthesis from sunlight, but also through dietary sources. Vitamin D is commonly consumed as a dietary supplement, and in some countries is also added to various food products. Though there is some debate on the cutoffs for deficiency and insufficiency, it is estimated that 50 to 60% of older populations worldwide are vitamin D deficient. As both vitamin D deficiency and increased adiposity have been associated with higher inflammation levels, the authors were interested in evaluating whether vitamin D supplementation might help lower inflammation levels in those trying to lose weight.

To do so, the authors utilized data from the Vitamin D diet and Activity (ViDA) clinical trial. This trial randomized 218 healthy postmenopausal women who were vitamin D insufficient (serum 25-hydroxyvitamin (25-OH) D level of 10-32 mg/mL) and overweight or obese, to receive either 2000 IU oral vitamin D3 supplementation/day or placebo. Over one year of study, both study arms also received a lifestyle-based weight loss program of diet and exercise, with a goal of losing 10% of their baseline weight. To measure the effect of this intervention on inflammatory biomarkers, the trial compared pre- and post-intervention serum measurements of leptin, adiponectin, the anti-inflammatory marker IL-10, and the pro-inflammatory cytokines TNF-α, IL-6, IL-1β, and IL-8.

At the end of the study, the average serum 25-OH-D levels increased 13.6 ng/mL in the vitamin D arm, but decreased by an average of 1.3 ng/mL in the placebo arm ($P < 0.0001$). While all of the inflammatory biomarker levels were reduced compared to baseline, these changes did not significantly differ between arms. To explore further, the authors performed analyses stratified by the degree of weight loss. Comparing those who lost at least 5% of their baseline weight to those who gained weight or did not lose weight, participants in the vitamin D arm had significantly greater decreases in IL-6 levels than those in the placebo arm (see figure).

These results suggest that weight loss and vitamin D3 supplementation may act synergistically to reduce IL-6 levels, at least among postmenopausal women who are vitamin D insufficient and overweight/obese. In vitro experiments have shown that the active form of vitamin D inhibits IL-6 production, and some hypothesize that weight loss may also increase the bioavailability of vitamin D in different tissues. Vitamin D supplementation did not, however, appear to lower other inflammatory cytokines beyond weight loss alone. Future studies are needed to further explore these potential relationships between weight loss, vitamin D intake, and inflammation.

Other PHS researchers contributing to this project were Drs. Jean de Dieu Tapsoba, Caitlin Mason, Ikuyo Imayama, Larissa Korde, and Ching-Yun Wang.

Duggan C, Tapsoba JD, Mason C, Imayama I, Korde LA, Wang CY, McTiernan A. 2015. Effect of Vitamin D3 supplementation in combination with weight loss on inflammatory biomarkers in postmenopausal women: a randomized controlled trial. *Cancer Prev Res* pii: canprevres.0449.2014. [Epub ahead of print]

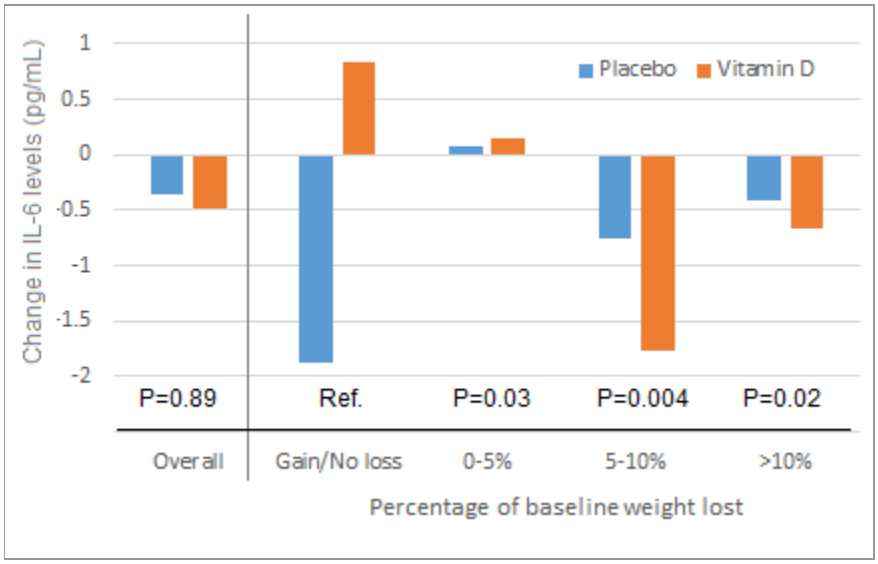

Image provided by Dr. Jonathan Kocarnik

Absolute change in IL-6 levels (pg/mL) from baseline to after a one-year weight loss intervention in the intervention arm (2000 IU/day vitamin D3) versus the placebo arm, overall and stratified by percentage of baseline weight lost. P-values are from covariate-adjusted generalized estimating equation models.