

Statins and Vitamin D—Conflict or Concord?

Although often ignored, the importance of food and drug interactions cannot be denied. The classic interactions of some cancer drugs and anti-seizure medications can lower the effectiveness of the medication. Grapefruit juice impacts the pharmacokinetics of *Lipitor* and other cholesterol-lowering medications (Bailey and Dresser, 2004).

Approximately 97% of those older than age 51 do not consume the current Adequate Intake of vitamin D (NHANES, 2005–06). In addition, as we age, ability to synthesize vitamin D declines (Oudshoorn et al., 2009),

health, neuromuscular functions, and numerous metabolic roles. A recent study indicated low levels of serum 25(OH)D₃ (≤ 15 ng/mL) are associated with more than twice the risk of cardiovascular disease and myocardial infarction in men relative to those with sufficient 25(OH)D₃ (≥ 30 ng/mL) (Giovannucci et al., 2008).

Several recent publications noted a relationship between the statins and vitamin D status whereas some studies indicate the absence of a relationship. Part of this relationship is that statins are HMG-CoA reductase inhibitors, and may inhibit the synthesis of 7-dehydrocholes-

et al., 2007). Another study among patients with acute coronary syndrome noted those receiving atorvastatin without additional vitamin D for 12 mo presented the expected improved lipoprotein profile and increased serum 25(OH)D₃ (18.8 ± 7.6 vs 16.4 ± 7.6 ng/mL) relative to the baseline (Pérez-Castrillón et al., 2007).

None of the apparent increases of serum 25(OH)D₃ levels in these studies achieved the concentration needed to reduce the risk of a cardiovascular event. However, with respect to bone health, a short-term study in Japan indicated patients

the 31 studies reviewed, there appeared to be small effects on some bone health biomarkers and no effect on others.

When patients receiving statin medication take vitamin D supplements, the interaction between vitamin D and the statin may have unexpected consequences (Schwartz, 2009). While the metabolic impact of vitamin D may reduce the risk of myocardial infarction and reduce the risk of hip fracture among the population receiving statin therapy, there is some evidence that vitamin D supplementation modulates the pharmacokinetics of the drug and its metabolites, while apparently exhibiting a synergistic lowering effect on cholesterol concentrations.

Perhaps vitamin D and its intermediates and the metabolites of statins have novel pleiotropic effects (Yavuz et al., 2009). These kinds of food and nutrient interactions with medications deserve increased investigation. Indeed they may explain some of the frequent variability when testing medications in clinical trials where nutrition is not considered an important factor. **FT**

Several recent publications noted a relationship between the statins and vitamin D status whereas some studies indicate the absence of a relationship.

as does the concentration of 7-dehydrocholesterol in the skin (MacLaughlin and Holick, 1985). This is the same population that is at risk for cardiovascular disease and prescribed the No. 1 HMG-CoA reductase inhibitor, atorvastatin, better known as *Lipitor* (Medical Expenditure Panel Survey, July 2007).

Vitamin D and cholesterol share a common metabolic pathway with 7-dehydrocholesterol (Holick, 2006). Upon transformation to 25-hydroxyvitamin D (25(OH)D₃) in the liver, there are several pathways through which this intermediate affects osteoblastic activity, calcium balance, and, ultimately, bone

terol and impair production of the active forms of vitamin D. The linkage of low vitamin D levels and cardiovascular disease has been suggested by in vitro studies demonstrating that vitamin D deficiency contributes to an imbalance of pro-inflammatory and anti-inflammatory cytokines, modulation of 25(OH)D₃ production, and abnormal sodium handling caused by perturbations of the renin-angiotensin system, which contribute to hypertension (Li, 2003).

A small study among women receiving vitamin D₃ for 2 years indicated that those on statins had a higher serum 25(OH)D₃ (20.5 ± 8.0 ng/mL) than those not on statins (17.3 ± 7.2 ng/mL) (Aloia

with heterozygous familial hypercholesterolemia who received step-wise doses of atorvastatin without vitamin D supplementation demonstrated a significant improvement in two bone metabolism markers. These same indicators were increased if these patients were treated specifically with vitamin D to achieve serum 25(OH)D₃ levels greater than 50 ng/mL (Kajinami et al., 2003).

A meta-analysis that examined the impact of HMG-CoA reductase inhibitors on osteoporosis indicated a reduced risk of hip fracture and improved hip bone mineral density (Hatzigeorgiou and Jackson, 2005). However, among



Roger Clemens, Dr. P.H.,
Contributing Editor
• Scientific Advisor,
ETHorn, La Mirada, Calif.
• rrclemens@ethorn.com



Wayne Bidlack, Ph.D., Contributing Editor
• Professor, California State Polytechnic University, Pomona
• wrbidlack@csupomona.edu