POINT - Counterpoint

Calcium and Vitamin D in Postmenopausal Women: Stones and Bones

We debated the use of vitamin D in postmenopausal women for the prevention of decreased bone mineral density, with Dr. Taylor presenting the “pro” side and Dr. Goldfarb the “con.” The controversial issue lies in whether vitamin D supplementation is likely to contribute to an increased incidence of kidney stones.

This topic was addressed in a recent article in The Journal of Urology® and an accompanying editorial. Most data suggest that vitamin D supplementation does not cause kidney stones. This relative safety is due to an increase in intestinal calcium absorption that suppresses the activity of 1-alpha-hydroxylase, the enzyme that catalyzes the conversion of 25-hydroxy vitamin D to active 1,25-dihydroxyvitamin D. This inhibitory effect should lead to the prevention of hypercalcemia and hypercalciuria, and protect against a resulting increase in kidney stones.

The “pro” side of the debate takes into account the seriousness of osteoporosis in the American population of postmenopausal women. Hip fracture occurs in more than 17% of U.S. women with a relative risk for mortality during the first 3 months after more than 5. Approximately 50% of people with hip fractures do not regain the ability to live independently. The relationship between calcium kidney stone formers specifically and increased rates of reduced bone mineral density is well-known.

Calcium supplements or calcium combined with vitamin D have a beneficial effect on bone density in postmenopausal women. Perhaps the benefit is more readily ascribed to calcium supplementation. For instance, in the Women’s Health Initiative the relative risk of hip fracture was 0.88 (95% CI 0.72-1.08). However, for adherent participants (predefined as those who took more than 80% of supplements) the relative risk was 0.71 (95% CI 0.52-0.97).

Perhaps the benefit would have been greater if the study included women with lower bone mineral density, or with lower calcium or vitamin D intake at baseline. Other variables that could have diminished the benefit were that 50% of women participants were taking hormone replacement therapy and that the control group was allowed to take supplements.

It is possible that the benefit would be greater in kidney stone formers. Data have shown that dietary calcium intake is less in men as well as in women with stones. A lower calcium intake is associated with a greater risk of stones. It is not clear exactly why there is an increased risk of stones in people taking calcium supplements while dietary calcium is associated with a reduction in stone incidence. However, it is possible that timing makes a difference.

Dietary calcium may serve as a binder of oxalate, thereby reducing oxaluria. Calcium tablets may not be administered with oxalate containing foods and, therefore, could lead to more calcuiura rather than reduced oxaluria. The result would be an increase rather than a decrease in urinary calcium oxalate supersaturation.

In a recent study, after multivariate adjustment (for numerous variables including use of calcium supplements), there was no statistically significant association between vitamin D intake and the risk of stones in a cohort of men or a cohort of older...
women.¹ A nonstatistically significant association was seen in a cohort of younger women.

The practical aspects of the data are that we recommend 1,000 to 1,200 mg total calcium daily for bone health. Most calcium should come from diet, with about 250 to 300 mg elemental calcium per 8 ounces of milk or yogurt, or calcium supplemented orange juice (an option for the lactose intolerant). If necessary, take calcium supplements with meals (during or up to an hour afterward), with calcium citrate being the preferred preparation. We do ensure vitamin D repletion in patients, with 20 to 30 ng/ml as the target.

In patients with kidney stones we recommend following the 24-hour urine calcium excretion, and have a low threshold for prescribing therapies for kidney stone prevention and low bone mineral density. Specifically, thiazides reduce urine calcium and increase bone mineral density and, thus, reduce the risk of fractures. Potassium citrate supplements also prevent stones, often reduce urine calcium slightly and cause an increase in bone mineral density.

However, in discussing this topic and the “con” side, it is necessary to point out that, to our knowledge, there are really no studies of vitamin D supplementation alone. In studies on vitamin D supplementation for the prevention of osteoporosis, it is always accompanied by calcium supplementation, which does appear to cause an increase in kidney stones. Such an effect was demonstrated in the Women’s Health Initiative, with an increase in the incidence of stones. In that population the absolute increase in stone incidence was low but the relative effect was near doubling.

The occurrence of vitamin D “toxicity” in the absence of very large ingestion is infrequent and could arise from the existence of loss-of-function mutations in CYP24A1. When that gene, which codes for 1,25-dihydroxyvitamin D24-hydroxylase cypochrome P450, is mutated, 1,25-dihydroxyvitamin D cannot be converted to the inactive calcitriol acid.

Individuals with biallelic or monoallelic mutations may present as adults with hypercalcemia, hypercalciuria, nephrolithiasis or kidney stones. Such affected individuals are different than idiopathic stone formers because of their low parathyroid hormone levels, high 1,25-dihydroxyvitamin D levels and low 24,25-dihydroxyvitamin D levels. Such individuals may account for the occurrence of vitamin D causing calcium stones.

However, the argument against vitamin D supplementation is less about the question of safety and more about the fact that screening for vitamin D deficiency is clearly overused. This inappropriate screening leads to excessive supplementation. Association studies have repeatedly shown that low vitamin D levels were associated with falls, fractures, cancer, high blood pressure and other adverse outcomes.

In addition, randomized trials of vitamin D supplementation failed to show significant benefit. Even in postmenopausal women with low 25-hydroxy vitamin D levels, supplementation offered little effect. Confusion in interpreting 25-hydroxy vitamin D levels also arises because of questions about the assays, varying recommendations about what values are considered desirable and seasonal variation in values related to exposure to sunlight.

As a result, the U.S. Preventive Services Task Force recommended against routine screening of vitamin D levels in adults who “are not known to have signs or symptoms of vitamin D deficiency or conditions for which vitamin D treatment is recommended.”¹³ Such patients would be those with established osteoporosis or chronic kidney disease. The American Board of Internal Medicine® Foundation has promoted its Choosing Wisely® initiative, and as a participant the American Society for Clinical Pathology recommended, “Don’t perform population based screening for 25-OH-Vitamin D deficiency.”¹⁵

A recent study demonstrated that requiring physicians to choose an indication for testing vitamin D reduced the number of tests ordered by 92%.⁶ So for many healthy people the question is not whether vitamin D causes kidney stones, but why they underwent screening and why they are taking vitamin D supplements at all.

Presented at this year’s AUA meeting in Boston, Massachusetts.