Long-term treatment of vitamin D insufficiency or deficiency in postmenopausal women does not increase urinary calcium excretion

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BACKGROUND

- Vitamin D insufficiency is widespread, affecting up to 40% of individuals in the U.S. and with prevalence rates approaching 80% in African Americans, Latinos, and postmenopausal women
- Low vitamin D status contributes to loss of bone density and fracture
  - **It also contributes to secondary hyperparathyroidism, a risk factor for calcium urolithiasis**
- Vitamin D and calcium are linked metabolically in that vitamin D is critical for calcium absorption
- The over-absorption of calcium can contribute to hypercalciuria and calcium stones
- Thus, vitamin D repletion in people who form kidney stones has been approached cautiously, even when vitamin D levels are low
- **The effect of long-term vitamin D repletion on urinary calcium excretion has not been well-studied**

OBJECTIVES

The aims of this post-hoc analysis of results from a randomized double-blind, placebo-controlled clinical trial were:

1) Assess the effect of long-term vitamin D repletion on urinary calcium excretion
2) Evaluate the response to repletion in individuals with pre-existing hypercalciuria

METHODS

- The objective of the original IRB-approved study was to compare effects of placebo, low-dose (LD) vitamin D, and high-dose (HD) vitamin D on changes at 1 year in vitamin D status, total fractional calcium absorption, and bone mineral density
- Postmenopausal women ≤75 years with baseline vitamin D [25(OH)D] levels of 14-27 ng/mL and no osteoporosis were eligible
- Subjects (n=90) were randomized to 1 of 3 study arms: (1) daily white and twice monthly yellow placebo **(placebo)**; (2) daily 800 IU vitamin D_3 and twice monthly yellow placebo **(LD)**; or (3) daily white placebo and twice monthly 50,000 IU vitamin D_3 **(HD)**
- 24-hour urine collections were provided when patients reported to the clinical research unit for overnight study visits at baseline (prior to intervention) and then at 60, 120, and 365 days

RESULTS

- **Urinary calcium excretion did not change at 1 year in either the HD or LD repletion group:**
  - 241 ± 75 to 230 ± 99 mg for all, *P*=0.46 unpaired; *P*=0.24 paired t-test
- Calcium absorption was not affected by treatment
- Blood levels of ≥30 ng/mL 25(OH)D were achieved and maintained only in women in HD treatment group
- Changes in urine calcium ranged from -15 to +20 mg/d and were not different between groups (**Figure 1**)
- Among all groups, 51 (57%) had hypercalciuria at baseline (≥200 mg/d) compared to 47 (52%) at 1 y
- At 1 year, calcium excretion decreased sufficiently to resolve hypercalciuria (**Figure 2**) in 25% of women
  - Resolution occurred in 19%, 36%, & 25% of women in the HD, LD, and placebo groups, respectively
- Urinary calcium excretion increased (**Figure 2**), resulting in new-onset hypercalciuria in 10 women
  - 2 in HD group, 5 in LD group, and 3 in placebo group
- Individuals' responses to vitamin D treatment were graphed (**Figure 3**)

Figure 1. Changes in urine calcium by VD repletion group

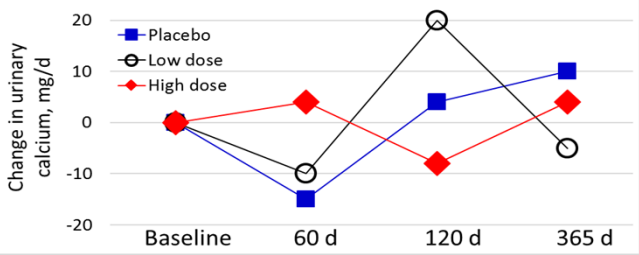


Figure 2. Changes in urine calcium in women with hypercalciuria

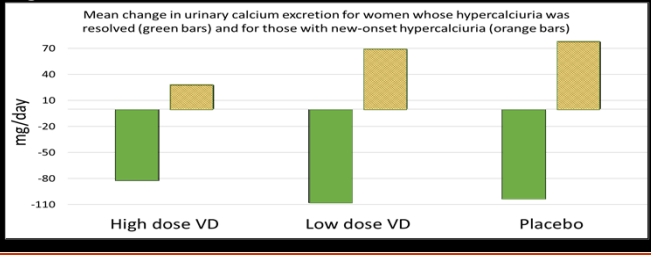
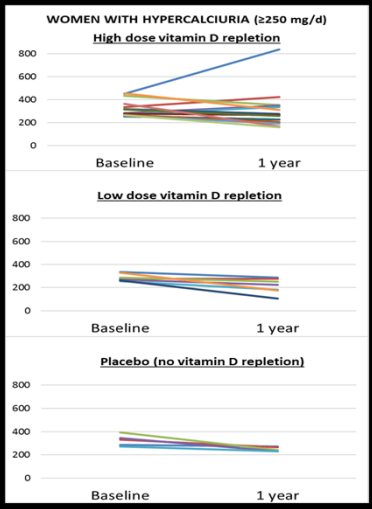


Figure 3. Individuals' responses



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CONCLUSIONS

- Vitamin D repletion in 60 postmenopausal women with vitamin D insufficiency did not result in higher urinary calcium excretion when compared to 30 vitamin D insufficient women who were randomized to placebo (not repleted)
- In women with hypercalciuria, urine calcium did not change with 1 year of vitamin D repletion (*P*=0.23 paired t-test)
- **Vitamin D repletion may have treated secondary hyperparathyroidism** among some women with vitamin D insufficiency
- As such, **our results may suggest a role for vitamin D repletion, appropriately prescribed, to reduce calcium stone risk**