Reviewer’s report

Title: Effects of vitamin D administration on cardiac natriuretic peptide levels in vitamin D deficient women

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Reviewer: Armin Zittermann

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This prospective study investigated the effect of oral vitamin D2 (either 50 µg daily or a single oral bolus of 1500 µg) on plasma NT-proBNP (a risk marker of cardiac dysfunction) in vitamin D insufficient lactating women. After 2 months, 25-hydroxyvitamin D concentrations were significantly higher and NT-proBNP concentrations were significantly lower compared to baseline.

Major compulsory revisions

The major problem with this investigation is its study design. This was not a randomized placebo controlled trial. Note that there are profound hormonal changes postpartum, including sex hormones and the vitamin D hormone calcitriol. Therefore, the reason for the decline in NT-proBNP remains unclear and can not be related to vitamin D supplementation.

The rationale for this investigation is unclear. Elevated levels of NT-proBNP are found in patients with cardiac diseases. However, these lactating women were apparently healthy. Others (Schleithoff et al., Am J Clin Nutr, 2006) did not find a decrease in NT-proBNP levels after vitamin D supplementation in patients with high NT-proBNP levels. Why has this article not been cited in the present manuscript?

The mean increase in 25-hydroxyvitamin D, which is the hallmark for determining vitamin D status, was relatively small (approximately 12 nmol/l). The mean 25-hydroxyvitamin D concentration was still in the insufficiency range (< 50 nmol/l) after 2 months of oral vitamin D2 supplementation. This seems surprising, since others have demonstrated that an oral daily vitamin D supplement increases 25-hydroxyvitamin D concentrations by 60 nmol/l (Schleithoff et al., Am J Clin Nutr, 2006). The oral bolus of 1500 µg should also have been high enough to result in a higher mean increase in serum 25-hydroxyvitamin D than only 12 nmol/l. The most likely explanation for this surprising result is the fact that they used vitamin D2 instead of vitamin D3. There is evidence that the increase in serum 25-hydroxyvitamin D is lower after vitamin D2 supplementation compared to vitamin D3 supplementation (Trang et al., Am J Clin Nutr 1998). Vitamin D2 should not be regarded as a nutrient suitable for supplementation or fortification (Houghton & Vieth R, Am J Clin Nutr, 2006).

Minor essential revisions
I am missing some important publications concerning vitamin D and cardiovascular disease (Zittermann et al., Br J Nutr, 2005) and natriuretic peptides (Zittermann et al., J Am Coll Cardiol, 2003; Schleithoff et al., Am J Clin Nutr, 2006).

Patients and Methods section, page 4, 25(OH)D measurement: Note that 25(OH)D is not a hormone.


Results section: The effect of vitamin D administration on serum 25-hydroxyvitamin D should be given separately for the groups that were supplemented with daily vitamin D2 and with the oral vitamin D2 bolus, respectively.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.