Reviewer's report

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

Version: 1 Date: 12 June 2008

Reviewer: Erin D Michos

Reviewer's report:

MAJOR COMMENTS

This study suffers from 2 major limitations which I think severely limit the interpretation and utility of this study. The authors mention both of these problems in their discussion but warrants further discussion as these are critical limitations. Perhaps if you could pull from other references (if available), it might help boost the meaning of your findings, but right now I am not sure we can make any useful inferences based on these major study design limitations.

1. There was no control arm of lactating women who did not receive any vitamin D. We have no idea that the fall in NT-proBNP levels was directly related to the vitamin D supplementation (vs some other factor such as weight loss as the women were farther and farther postpartum with time). Are there any other studies that looked at cardiac natriuretic peptide levels in peripartum women that we can extrapolate from? Why did you choose to do this study in the lactating women rather than the nulliparous women in your reference 8? In the nulliparous women, it would have been more believable that a fall in NT-proBNP might be related to vitamin D supplementation since you could anticipate their weights to be relatively stable over a 2 month period. But 25(OH)D levels are strongly associated with weight, so in lactating women postpartum, I have no reason to believe that a change in NT-proBNP has anything to do with vitamin D supplementation vs simply time from delivery.

2. You said that these lactating [and thus I presume they were young (although no mean age was given)] women had normal levels of NT-proBNP and PRA at baseline. Thus I suspect they did not have clinical heart failure at baseline. Can you reference any data that suggests that lowering cardiac natriuretic peptide levels in women without heart failure and with normal baseline levels has any clinical benefit??? In your dialysis population (reference 19) which already has elevated levels, I can see how this might be beneficial. But in normal women, what is the clinical utility of lowering levels even further?? You didn’t even find an association between 25(OH)D levels and cardiac natriuretic peptide levels in this cohort. As you state yourself, “physiological significant an unresolved issue”.

Other MAJOR Comments

3. There is no Table I with the baseline characteristics such as important characteristics such as mean age, blood pressure, BMI – all of which are factors
which are associated with 25(OH)D levels. This is a gross oversight – as how are we to extrapolate the results to other populations if this study population is not even described! While reference is made to earlier publication (reference 8), that study had 90 lactating and 88 nulliparous women while this only had around ~50 lactating women, so it is not exactly the same cohort sample. Thus we should have some summary of clinical characteristics of the women included in these analyses.

4. You said in your methods that this was a randomized clinical trial. Lactating women were randomized to receive oral vitamin D2 either 2,000 daily or 60,000 IU monthly. Was there any difference in the cardiac natriuretic peptides between the daily dosing vs monthly dosing? Did one vitamin D regimen raise 25(OH)D levels or lower NT-proBNP levels better than the other regimen?

5. While there was no association of 25(OH)D with NT-proBNP or PRA at baseline, was there any correlation between 25(OH)D levels with NT-proBNP and PRA at followup? This should be reported. If there is no correlation, then if the reduction in NT-proBNP is causally related to vitamin D therapy (and not just time postpartum), then how do you explain this?

Minor comments

6. In the methods section, you describe where the assays for NT-proBNP and 25(OH)D were run and the interassay variability. However you do not mention how/where the samples for plasma renin were measured and the interassay variability for PRA.

7. In the United States and many European countries, vitamin D levels vary dramatically by season. Thus 25(OH)D analyses are often adjusted by season of lab draw. Did you see any seasonal variability of 25(OH)D levels in your cohort?

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.

Declaration of competing interests:

I have received a one time minor honorarium fee for participating in a symposium sponsored by Abbott, who makes zemplar. I have no on-going relationships, never had any significant relationships, have no financial competing interests.