Reviewer's report

Title: The impact of vitamin D supplementation on vascular stiffness and blood pressure in Chronic Kidney Disease patients

Version: 2
Date: 15 July 2014

Reviewer: Ishir Bhan

Reviewer's report:

This manuscript describes a placebo-controlled, 3 arm, randomized trial that intends to examine the effects of two forms of vitamin D on vascular stiffness using pulse wave velocity. My main concerns with this manuscript are the lack of citations for previous work in this area (including clarification of what this study adds, and lack of clarify in the details of the study.

Major compulsory revisions

The abstract should state that the trial is randomized.

The manuscript, including the abstract, often refers loosely to “vitamin D” without clarification as to which form is being discussed.

In the background, the contribution of LVH, which is highly prevalent in CKD, should be discussed with respect to cardiovascular disease in addition to athero/arterosclerotic processes.

It is an overstatement to say that “vitamin D deficiency is regarded as an important cardiovascular risk factor” both in the abstract and background. There have been links of vitamin D levels with outcomes, but little trial data. The data since the cited 2007 meta analysis have largely been negative.

To say that patients with CKD “lack 25-hydroxyvitamin D” is misleading. It’s not totally absent, just ends to be low. It’s also not accurate to say that they “lack the physiological capacity to hydrolyze 25 vitamin D into its active form”. First of all, the capacity is reduced, not absent. Second of all, the enzymatic step is hydroxylation, not hydrolysis.

Hewitt et al (Clin J Am Soc Nephrol, 2013) looked at pulse wave velocity and other measures and found no effect as part of a randomized trial. This should be cited.

Pulse wave velocity was examined in a study by Marckmann et al. (Nephrol Dial Transplant, 2012). This should be referenced. What does the proposed study add? The same can be said about the study by Gepner et al., PLoSOne, 2012). Given that studies of PWV and vitamin D supplementation have been performed before, the authors should review the existing literature on the topic and clarify what the proposed study adds. I am not convinced this is novel.
The hypothesis is not clear. It is statement that vitamin D analogues will result in “greater changes in PWV measurements than placebo”. Is PWV expected to increase or decrease?

The methods also need clarification: are D2 or D3 forms of vitamin D being used? Is a supplement of 25-OH vitamin D actually being used, or is it nutritional vitamin D (e.g. ergo or cholecalciferol) where you are relying on the liver to perform the 25 hydroxylation. 25-OH vitamin D is not commonly used or available in supplemental form.

The PRIMO study is referenced, but the outcome cited (CV hospitalization) was not the primary endpoint: the trial overall was negative. This should be clarified.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests