Reviewer's report

Title: Low-dose menaquinone-4 improves gamma-carboxylation of osteocalcin in young males

Version: 1 Date: 4 May 2014

Reviewer: Kiyoshi T. K. Tanaka

Reviewer's report:

(1) General comments
In this paper, the authors have made the intervention studies with graded doses of menaquinone-4 (MK-4) with serum undercarboxylated osteocalcin (ucOC) level, a marker for skeletal vitamin K deficiency, as the endpoint. As the authors state in the Introduction and Discussion, vitamin K requirement is considered to be much higher in the bone than in the liver, yet the intervention study for skeletal dose requirement has not been reported.

(2) Major revision
1. Data on vitamin K intake (Table 2) have something strange. Median dietary vitamin K intake is approximately 50 microgram/week, which is incredibly low and inconsistent with their description that the vitamin K intake was similar to DRIs (line 109-110). Table 2 also shows the presence of the subject(s) with null vitamin K intake, which is quite difficult to imagine. Vitamin K intakes on day 29 and 36 are markedly decreased.

Additionally, what was the vitamin K intake at baseline?

2. The authors have made some discussion citing the Dietary Reference Intakes for Japanese 2010. Reference #7 is a book in Japanese. I think that citing the paper below, one translated to English, would be more suitable for the foreign readers.


Additionally, DRIs 2015 was released on March 31, 2014. Since their work was done before that, I think that making the discussion with regard to DRIs 2010 is not a major problem. The authors are advised, however, to mention the new DRIs.

3. The authors have made the statistical analyses using Kruskal-Wallis test. This is a non-parametric test for unmatched sample. Since the data here are matched ones, I think that Friedman's test is to be employed.

4. The authors are advised to comment on the decreased PK level after the intervention.
(3) Minor comments
1. Dietary Reference Intakes is usually used in the plural form, not Dietary Reference Intake (line 35, 106).

2. The description “each country determines a dietary reference intake or adequate intake” is rather confusing. Adequate intake is one of the parameters in the DRIs.

3. The authors state that larger amount of vitamin K may be needed (line 36). What do they mean by “larger”? Larger than what?

4. The authors have mentioned a previous epidemiological study citing reference #7. Since this is a guideline, citing the original paper is recommended. If the authors prefer to cite this guideline, I think that it would be better written as below.

Based on an epidemiological study on serum ucOC levels, recently published guideline recommends the daily vitamin K intake of 250 to 300 micrograms.

5. Also, the original paper should cited instead of the guideline at line 113.

7. AI for vitamin K is 75 microgram/day for adult men, and 65 microgram/day for adult women in the DRIs for Japanese 2010. Specify the gender at line 108.

8. Reference in Japanese are advised to be specified.

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.