Reviewer’s report

Title: Changes in the vitamin D endocrine system and bone turnover after oral vitamin D3 supplementation in healthy adults: Results of a randomised trial

Version: 1 Date: 12 March 2012

Reviewer: Gunnar Sigurdsson

The objective of this study was secondary to a previously published study on the increase in s-25(OH)D using fish oil capsules and multivitamin D-tablets. In this study the authors present predefined secondary objectives to compare changes in s-1,25(OH)2D, s-iPTH and s-TRACP using standardized methods.

This is a randomized study, but the study group is rather heterogeneous, consisting of 55 individuals, men and women, 36 of Norwegian background, 12 of Tamil background, and seven of various other ethnic backgrounds. The baseline s-25(OH)D ranged from 12 nmol/L to 58 nmol/L, 14 out of 55 participants had s-25(OH)D <25 nmol/L and might therefore be reaching osteomalacia values.

Major Compulsory Revisions

The study subjects were recruited primarily among medical and nursing students in Oslo, ranging from the age 19-48, but 40% were younger than 25 years of age. The intervention started in mid-February 2005, but it is not mentioned how long the incubation period lasted, which could be of significance with regard to s-25(OH)D values.

Results

The participants completed a questionnaire at baseline, including vitamin D containing foods, and the number of participants taking different items is listed as percentage in table I. However, no estimate of total vitamin D intake is mentioned, which might be of interest, especially in comparison between the ethnic groups in that respect.

The main increment in s-25(OH)D in both study groups was similar, about 8 nmol/L per 100 units of vitamin D which is considerably higher than many other studies have found. This might suggest other effect than of the supplementation per os. Therefore it is of importance to clarify the time period of the study, when the last blood samples were taken.

The authors found a significant decrease in s-iPTH and the decrease did not differ significantly by type of supplement. They observed a large variation in the increment in s-1,25(OH)2D. As an estimate of bone turnover they used s-TRACP but no other estimates such as alkaline phosphatase or osteocalcin. They found that s-TRACP increased significantly during supplementation. This assay measures the active isoform 5b derived from osteoclasts and as the authors
mention in the discussion, this enzyme is specifically a marker of number of osteoclasts rather than of their resorptive activity. The Tamils had higher baseline s-TRACP and had higher increase during supplementation which the authors claim was not significant when adjusting for higher baseline values. As other studies have shown, they found a stronger PTH suppression after supplementation in those who had lower vitamin D status at baseline (fig.1).

From those results the authors conclude that the effect of four weeks of daily supplementation with 10 µg (400 IU) of vitamin D3 did not differ by mode of administration. This conclusion with regard to decrease in s-iPTH seems to be sound. However, the conclusion that there is an increase in bone turnover as measured by s-TRACP is another matter as the study group was so heterogeneous in terms of age, ethnic background and baseline values in s-TRACP. Further comparison between the sub-groups (which might be difficult to perform because of small numbers) is needed to justify such conclusions. As mentioned above and the authors refer to, young people differ in the response and participants with extremely low s-25(OH)D (possibly with evidence of osteomalacia) respond differently, such as is known from the alkaline phosphatase flare in such individuals. Without other measurements of bone turnover it is hardly justified to make such conclusions but the results may show such tendency with regard to s-TRACP whatever that means.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

No conflicting interests