Reviewer’s report

Title: The effects of single high-dose or daily low-dosage oral colecaciferol treatment on vitamin D levels and muscle strength in postmenopausal women

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Reviewer: Martin Hewison

Reviewer’s report:

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The manuscript by Apaydin et al describes a relatively straightforward but nevertheless interesting study in which the authors have compared the impact of two different vitamin D supplementation regimens on serum vitamin D 'status' and muscle function in a cohort of postmenopausal women who were vitamin D-deficient (< 50 nmol/L) at the start. The two types of vitamin D supplementation used in the study were: 800 IU/day or 300,000 IU single dose. Rather predictably the latter regimen was better at increasing serum 25-hydroxyvitamin D (25D) than the former, although both increased 25D relative to baseline. However, muscle function appeared to improve only in the group receiving daily dosing with vitamin D. These observations provide plenty of talking points, but to make these meaningful talking points, the authors need to perhaps do some additional analyses and some data reorganisation.

Specific comments:

1. The crucial observation from this study is that simply elevating serum does not guarantee success with vitamin D supplementation. The authors need to provide more information on why this occurs. One possibility is that the different dosing regimens have different effects on vitamin D metabolites other than serum 25D. Are serum 1,25-dihydroxyvitamin D (1,25D) or 24,25-dihydroxyvitamin D (24,25D) different? Measuring these metabolites is more work but it may provide crucial new information. For example recent studies have shown that muscle function in humans correlates more closely with 1,25D than 25D. Is 1,25D higher with the daily dosing? Or, indeed, is the catabolic metabolite 24,25D higher with the single large dose - this has been suggested previously. The authors should measure other serum vitamin D metabolites

2. The authors should re-structure Table 2 to place the Single Dose and Daily Dose data side-by-side. This will allow much easier comparison of these two sets of data.
3. In Table 4 the authors have stratified data according to serum 25D level (<20, >20, <30, >30). This stratification should be applied to the muscle function data. In other words at week 4 the single dose group had many more women >30 ng/ml serum 25D but this did not have a dramatic effect on muscle function. Therefore which group of women from the daily dosing saw the most improved muscle function - those < 20, those >20???

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
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Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
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