



Comments on Minisola et al.: Correction of vitamin D status by calcidiol: pharmacokinetic profile, safety, and biochemical effects on bone and mineral metabolism of daily and weekly dosage regimens

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Dear Editor,

We thank Dr. Minisola et al. [1] for sharing their significant study indicating that correction of vitamin D status by calcidiol: pharmacokinetic profile, safety, and biochemical effects on bone and mineral metabolism of daily and weekly dosage regimens. In this study, 87 Caucasian postmenopausal women with vitamin D inadequacy were randomized to receive three different dosages of calcidiol for 3 months. Serum 25(OH)D and other parameters of mineral metabolism were assessed to establish efficacy and safety. However, we have several concerns about this study.

First, patients in the group of 40 µg/day had always higher serum 25(OH)D level than did patients in any other two groups throughout the study. Meanwhile, vitamin D-binding protein in the patients of 40 µg/day had a significant increase as compared with their baseline level. Since the free hormone hypothesis postulates that protein-bound hormones are biologically inactive, unbound hormones are biologically free to exert their activity [2]. We recommend that free 25(OH)D level should be considered and calculated, when investigating the efficacy and safety of vitamin D supplement.

Second, it was very interesting that although higher 25(OH)D increment was observed in the group of 40 µg/day, the different dosages were equally effective in controlling secondary hyperparathyroidism at the end of the study. This would address one question that the change of PTH level was

just partially dependent on total 25(OH) D level. To clarify the associations between change in iPTH and change in total or free 25(OH)D, and 1,25(OH)D, we recommend that linear regression model should be performed with supplementation regimen, change in 1,25(OH)D, 25(OH)D, and change in calcium as covariates [3]. This would be helpful for us to find out the best cost-effective way to supplement calcidiol in clinical practice.

Finally, as we all know, vitamin D status is often influenced by sunshine and fortified food or drinks. The authors should specify how often for outdoor activity and any fortified vitamin D supplement in each group.

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Compliance with ethical standards

Conflicts of interest None.

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A response to these comments can be found at <https://doi.org/10.1007/s00198-018-4398-8>.

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