LETTERS TO THE EDITOR

Vitamin D₂ and vitamin D₃ comparisons: fundamentally flawed study methodology

Dear Sir:

The recent article by Biancuzzo et al (1) presents data showing that vitamin D is equally bioavailable from orange juice and gel caps. This equivalence of vehicle was shown for both vitamin D₂ and vitamin D₃. The article is important because it has implications for health policy. However, health professionals, scientists, and the public alike are interpreting this article as evidence that vitamin D is equally bioavailable from orange juice and gel caps. This interpretation is incorrect—vitamin D₂ is equally as effective as vitamin D₃ in both orange juice and in capsular form in raising and maintaining total serum 25-hydroxyvitamin D [25(OH)D₃] concentrations and thus the results were not ambiguous—ie, vitamin D₂ was equally as effective as vitamin D₃ in both orange juice and in capsular form in raising and maintaining total serum 25(OH)D. We have performed a direct comparison of the area under the curve (AUC) for both total serum 25(OH)D₃ concentrations and individually for serum 25(OH)D₂ and 25(OH)D₃ concentrations. In our article (2), we clearly showed that serum 25-hydroxyvitamin D₂ [25(OH)D₂] and 25-hydroxyvitamin D₃ [25(OH)D₃] increased in identical fashion, and thus the results were not ambiguous—ie, vitamin D₂ was equally as effective as vitamin D₃ in raising and maintaining serum 25(OH)D concentrations and individually for serum 25(OH)D₂ and 25(OH)D₃ concentrations. We looked at total 25(OH)D₃ AUC [25(OH)D₃]+25(OH)D₂] for the postbaseline period, and compared the combined group who received doses with vitamin D₃ (OJ+gelcaps) with the combined group who received doses with vitamin D₂ (OJ+gelcaps). For the 38 subjects who received doses with vitamin D₃, the mean (±SD) AUC for total 25(OH)D was 286.28 ± 93.57. For the 33 subjects who received doses with vitamin D₂, the mean (±SD) AUC for total 25(OH)D was 259.82 ± 74.28. There was no significant difference between these 2 groups in mean total 25(OH)D AUC (P = 0.196, independent-samples t test).

We also evaluated the difference in mean total 25(OH)D AUC between the original 5 randomization groups. The analysis results show a significant overall group difference in mean total 25(OH)D AUC (P = 0.0406, ANOVA F test), but post hoc testing indicated that the only significant pairwise comparison was between the placebo (PL) and OJ(D₃)+PL groups; there were no significant differences in the mean total 25(OH)D AUC between the 4 groups treated with either vitamin D₃ or vitamin D₂ (Table 1). Therefore, on the basis of all of these analyses, it can be concluded with a high degree of certainty that vitamin D₂ is equally as effective as vitamin D₃ in raising and maintaining serum total 25(OH)D concentrations and that vitamin D₂ is equally as bioavailable as vitamin D₃.

The authors had no conflicts of interest to declare.

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Reply to S Lanham-New et al

Dear Sir:

We were pleased that Lanham-New et al appreciated that this article has important implications for health policy. It is, however, surprising and disappointing that these 3 experts did not fully understand the design, outcomes, and conclusions of our study. This study was designed to compare not only the bioavailability of vitamin D₂ and vitamin D₃ in orange juice with that in capsules, but it also was designed to confirm the previous report (1) that vitamin D₂ is equally as effective as vitamin D₃ in raising and maintaining total serum 25-hydroxyvitamin D [25(OH)D] concentrations. In our article (2), we clearly showed that serum 25-hydroxyvitamin D₂ [25(OH)D₂] and 25-hydroxyvitamin D₃ [25(OH)D₃] increased in identical fashion, and thus the results were not ambiguous—ie, vitamin D₂ was equally as effective as vitamin D₃ in both orange juice and in capsular form in raising and maintaining total serum 25(OH)D. We have performed a direct comparison of the area under the curve (AUC) for both total serum 25(OH)D concentrations and individually for serum 25(OH)D₂ and 25(OH)D₃ concentrations. We looked at total 25(OH)D₃ AUC [25(OH)D₃]+25(OH)D₂] for the postbaseline period, and compared the combined group who received doses with vitamin D₃ (OJ+gelcaps) with the combined group who received doses with vitamin D₂ (OJ+gelcaps). For the 38 subjects who received doses with vitamin D₃, the mean (±SD) AUC for total 25(OH)D was 286.28 ± 93.57. For the 33 subjects who received doses with vitamin D₂, the mean (±SD) AUC for total 25(OH)D was 259.82 ± 74.28. There was no significant difference between these 2 groups in mean total 25(OH)D AUC (P = 0.196, independent-samples t test).

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None of the authors declared a conflict of interest.

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