Reviewer's report

Title: Postprandial effects of calcium phosphate supplementation on plasma concentration-double-blind, placebo-controlled cross-over human study

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Reviewer: Robert P Heaney

Reviewer's report:

This is a well-designed and well-executed study and, given the continuing concern about potential harmful effects of phosphorus intake, it is, as well, a potentially important study. The authors show that, either acutely, or after chronic feeding, calcium phosphate does not elevate serum phosphorus, and hence would not be expected to contribute to the problem of ectopic calcification.

There are, however, several issues that need to be dealt with, but which should present no difficulties for the authors.

• First, although the authors provide information with respect to the total daily load of calcium phosphate, and the Tables give the load size for the oral tests, both the text and the Abstract are silent on the size of the calcium or phosphorus loads used for the single test dose for which they were able to assess the time course following ingestion. This is a vital piece of information and is essential for interpreting the results as well as for comparing with the reports of other studies, as in the first paragraph of the Discussion section.

• The calculation of the AUC for both calcium and phosphorus is incorrect, inasmuch as the AUC should be based on the increment/decrement above/below baseline, not on the total concentration of calcium or phosphorus. The authors can see this very clearly when they contrast the fact that there was a significant elevation in serum calcium and a significant decrease in serum phosphorus; yet if they compare the AUC values between placebo and calcium phosphate, I suspect they would find no significant difference, i.e., using AUC only they would have had to report no effect for either serum calcium or serum phosphorus. On the other hand, I predict that the incremental AUCs will differ significantly, and therefore, will contain important information about the response. The current AUC illustrations should be revised.

Minor Comments

• Phosphorus is misspelled throughout the manuscript.

• The authors omit an important, if not actually demonstrated, mechanism for the hypophosphatemia following ingestion. That is the secretion of calcitonin which follows from release of gastrointestinal hormones upon ingestion of a meal. This would have produced an immediate cessation of osteoclast work, and hence a fall in release of phosphorus into the blood from bone. The calcitonin effect is likely the cause for the phosphorus decrement in the placebo group. That, and the immediate increase in renal phosphorus clearance that accompanies a fall in
PTH, would be predicted to lower serum phosphorus concentration appreciably. This strikes the reviewer as substantially more plausible than hydration, which, had it been the cause of the drop in serum phosphorus, should have produced a corresponding drop in red cell count.

• The paper would be enhanced if the authors would calculate and present the $Ca \times P$ ion product at all time points around the test meal.

• Although the authors quote a study by Heaney with respect to phosphorus absorption, they might also wish to look at the papers by Rafferty et al. (J Food Sci 72:152-158, 2007) or Heaney et al. (Calcif Tissue Int 46:300-304, 1990). Both contain additional information about measured phosphate absorption.

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 interest.