Calcium Acetate versus Calcium Carbonate as Phosphate Binders

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Dear Sir,

Two recent papers comparing calcium carbonate with calcium acetate both conclude that calcium acetate is the better phosphorus binder. In the paper by Caravaca et al. [1], the serum phosphate concentration was 1.80 ± 0.50 (SD) mmol/l while on calcium acetate, and 1.93 ± 0.48 on calcium carbonate in a parallel study on 31 plus 35 patients. Using the pooled estimate of variance,

$\text{Var}_{\text{diff}} =$

$\text{SD}_1^2 \cdot (n_1 - 1) + \text{SD}_2^2 \cdot (n_2 - 1) / (n_1 + n_2 - 2)$

and $\text{SE}_{\text{diff}} = \sqrt{\text{Var}_{\text{diff}}}$

the standard error on the difference is readily obtained as 0.121 mmol/l and hence a 95% confidence interval of -0.37 mmol/l to 0.11 mmol/l, i.e. a nonsignificant difference. The authors report a significant increase from 1.77 ± 0.35 (while on aluminum hydroxide) to 1.93 ± 0.48 mmol/l on calcium carbonate, with $p = 0.03$ using a paired t test. In contrast, a nonsignificant increase from 1.73 ± 0.25 to 1.80 ± 0.50 mmol/l was found comparing aluminum hydroxide to calcium acetate. From that, the authors conclude that calcium acetate is better. In the first t test, however, we can see that t must have been 2.2650, and the standard error of the mean difference therefore $(1.93 - 1.77)/t$, that is 0.07064. Likewise, the standard error in the second test is 0.06097. Since the standard deviations in the two differences can be computed as the square root of the group size multiplied by the standard errors of the means above and since a pooled estimate of the variance of the difference between the two differences and the relevant standard error of the mean difference can be found as above, an unpaired t test of the difference between the difference yields

$t = (1.93 - 1.77) - (1.80 - 1.73) / 0.0945$

With 64 degrees of freedom this gives a p value of 0.35. Hence, the authors' informal comparison of a significant with an insignificant change appears to be mistaken. In the paper by Morinière et al. [2] 8 patients were compared while being treated with half the dose of elemental calcium as calcium acetate compared to calcium carbonate. The authors were unable to find a difference between 1.74 ± 0.32 mmol/l (on calcium carbonate) and 1.75 ± 0.38 mmol/l (second course of calcium acetate). The power of the paired t test used was not specified. Hence it is difficult to accept this as a proof of the superiority of calcium acetate, especially since more magnesium hydroxide was given with calcium acetate. An estimate of the confidence interval is obtained using the relation

$\text{CI}_{\text{diff}} = \sigma_1^2 + \sigma_2^2 - 2 \cdot \sigma_1 \cdot \sigma_2 \cdot \rho$ (1,2),

where p is the correlation between measurements on aluminum hydroxide and calcium carbonate or calcium acetate. Inserting the standard deviations given above in the paper by Caravaca et al. [1] in the two comparisons, correlations of 0.53 and 0.79 are obtained. Using 0.79 (which gives the narrower confidence interval), the standard error of the mean difference in the paper by Morinière et al. [2] is obtained as
 $= 0.0826$.

$$\frac{1}{0.322 + 0.382 - 2 \times 0.32 \times 0.38 \times 0.79}$$

With 7 degrees of freedom, t corresponding to a 95% confidence interval is 2.365. Hence the confidence interval for the difference in phosphate concentration is -0.19 to 0.21 mmol/l. The superiority of calcium acetate therefore implies that one does not consider a possible difference of 0.21 mmol/l to be important.

References

- Caravaca F, Santos I, Cubero JJ, et al: Calcium acetate versus calcium carbonate as phosphate binders in hemodialysis patients. *Nephron* 1992;60:423-427.
- Morinière Ph, Djerad M, Boudailliez B, et al: Control of predialytic hyperphosphatemia by oral calcium acetate and calcium carbonate. *Nephron* 1992;60:6-11.