Survival differences between activated injectable vitamin D_2 and D_3 analogs

Kidney International (2007) **71,** 827. doi:10.1038/sj.ki.5002208

To the Editor: In the study by Tentori *et al.*,[1] even though the crude mortality of dialysis patients who received vitamin D_3 analog *calcitriol* was inferior to those who received either of the two vitamin D_2 analogs *paricalcitol* or *doxercalciferol*, these differences were not statistically significant after multivariate adjustment.[1] In contrast, Teng *et al.*[2] had reported a robust survival advantage of vitamin D_2 *paricalcitol* compared with vitamin D_3 *calcitriol* irrespective of multivariate adjustment. Tentori's different findings may be related to several cohort characteristics:

(1) The median time on hemodialysis before the first vitamin D_3 administration was significantly shorter (18 days) compared with D_2 analogs (37 days, $P<0.0001$).[1] Assuming that there is a survival advantage of any vitamin D compared to no vitamin D at all, as found by the same authors[1] and others,[3–5] the twice longer period of time without any vitamin D in the D_2 groups could have led to residual inferior survival in this group to the extent that subsequent superior survival of vitamin D_2 administration was irreparably mitigated.

(2) Prior to vitamin D analog administration, the D_2 groups had significantly higher baseline serum calcium, phosphorus, and PTH values, all of which are associated with higher death risk.[4,6]

(3) Patients in D_2 groups had significantly shorter follow-up time when compared with the D_3 group, as evident in the Kaplan–Meier survival graphs.[1] Longer cohort times could have resulted in more consistent survival differences between D_2 and D_3 groups.

Despite the foregoing and other limitations such as the large proportion of African Americans and unusually large number of patients who never received any vitamin D analog, Tentori *et al.*[1] still found a greater survival trend in the D_2 (paricalcitol and doxercalciferol) groups compared with D_3 (calcitriol) group. It would be interesting to know whether a more commensurate comparison, for example, a matched study that would only include patients with shorter pre-D_2 period with lower serum minerals and PTH and longer follow-up periods in the D_2 groups as in the D_3 group would have resulted in even larger survival advantages of D_2. The Tentori study[1] should still be considered as yet another evidence that administration of any active vitamin D analog, especially if D_2, may confer improved survival to maintenance dialysis patients.

1. Tentori F, Hunt WC, Stidley CA *et al.* Mortality risk among hemodialysis patients receiving different vitamin D analogs. *Kidney Int* 2006; **70**: 1858–1865.
2. Teng M, Wolf M, Lowrie E *et al.* Survival of patients undergoing hemodialysis with paricalcitol or calcitriol therapy. *N Engl J Med* 2003; **349**: 446–456.
3. Teng M, Wolf M, Ofsthun MN *et al.* Activated injectable vitamin d and hemodialysis survival: a historical cohort study. *J Am Soc Nephrol* 2005; **16**: 1115–1125.
4. Kalantar-Zadeh K, Kuwae N, Regidor DL *et al.* Survival predictability of time-varying indicators of bone disease in maintenance hemodialysis patients. *Kidney Int* 2006; **70**: 771–780.
5. Lee GH, Benner D, Regidor DL *et al.* Impact of kidney bone disease and its management on survival of patients on dialysis. *J Ren Nutrition* 2007; **17**: 38–44.
6. Block GA, Klassen PS, Lazarus JM. Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. *J Am Soc Nephrol* 2004; **15**: 2208–2218.

K Kalantar-Zadeh[1,2]
[1]Division of Nephrology and Hypertension, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California, USA and [2]David Geffen School of Medicine at UCLA, Los Angeles, California, USA
Correspondence: *K Kalantar-Zadeh, Division of Nephrology and Hypertension, Harbor-UCLA Medical Center, 1124 West Carson Street, Torrance, California 90502, USA. E-mail: kamkal@ucla.edu*

Response to 'Survival differences between activated injectable vitamin D_2 and D_3 analogs'

Kidney International (2007) **71,** 827–828. doi:10.1038/sj.ki.5002218

We appreciate Dr Kalantar-Zadeh's letter. Our study had two major findings. First, mortality was reduced among hemodialysis (HD) patients treated with intravenous vitamin D. Second, the mortality risks associated with administration of paricalcitol versus doxercalciferol were similar.

Administration of paricalcitol and doxercalciferol was associated with a significant survival benefit compared with calcitriol only in the unadjusted model and in the model adjusted for demographics. Dr Kalantar-Zadeh[1] postulates that these findings reflect differences among patients receiving the respective vitamin D preparations. Time on HD before vitamin D administration was longer in patients receiving paricalcitol (37 days) or doxercalciferol (37 days) versus calcitriol (18 days). Baseline concentrations of calcium (paricalcitol and doxercalciferol: 8.8 mg/dl; calcitriol: 8.5), phosphorus (paricalcitol and doxercalciferol: 5.1 mg/dl; calcitriol: 5.0), and PTH (paricalcitol: 318; doxercalciferol: 335 pg/ml; calcitriol: 289) were higher among patients receiving paricalcitol and doxercalciferol versus calcitriol. However, it seems unlikely that these modest differences were clinically significant. Similar differences were observed by Teng *et al.*[2] The median follow-up times were longer among the calcitriol (41 weeks) versus the paricalcitol (39 weeks) and doxercalciferol (32 weeks) treated groups, but it is unlikely