Title
Response to ‘Osteodystrophy and dialysis survival’

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declared that, 'The evidence is here,' in reference to a Wyeth product. These bands convey the impression of a connection between scientific evidence for the products, the pharmaceutical company, and the independent academic journal.

The November editions of the *Journal of the American Society of Nephrology, American Journal of Kidney Diseases*, and *Kidney International* contained 30, 19, and 13 advertisements, respectively. Of these three journals, the November issue of *Kidney International* actually had the lowest number of large page advertisements. However, unlike these other journals, advertisements in *Kidney International* were not limited to the pages preceding and following the contents of the journal but were interspersed. These observations raise the question of whether journals face a trade-off between running a larger number of appropriate advertisements or a lesser number of (presumably more lucrative) inappropriate advertisements in order to cover costs.

To avoid risking the loss of respect of its readers, we urge *Kidney International* to eliminate practices that blur the boundary between academic pursuits and advertising. If we are incapable of self-regulation, it will only be a matter of time before the government steps in to control advertising practices in medical journals.

1. The New York Times Company Journalism Ethics Policy http://www.nytco.com/company-journalism-ethics.html.

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Osteodystrophy and dialysis survival

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To the Editor: In the article by Kalantar-Zadeh [1] we noticed with interest that the survival benefit granted by paricalcitol paradoxically decreased with higher doses. Since the latter doses are more likely to be hyperphosphatemic and hypercalcemic, this suggests that these deleterious side effects counterbalance the beneficial effects of paricalcitol related to partial correction of the usual vitamin D depletion of the American Dialysis population. Indeed vitamin D deficiency has been epidemiologically related to a higher risk of diabetes and cardiovascular risk by activation of inflammation and this can simply be suppressed by plain vitamin D administration.[2] This simple measure can furthermore quite efficiently suppresses parathyroid hormone (PTH) and allow to limit the dose of the more potent (inappropriately called 'active') vitamin D derivatives, while decreasing the risk of calcification. This is strongly suggested by the comparison of 2 cohorts of young adults with childhood onset of end-stage renal disease (ESRD):[3,4] the Berlin cohort [4] had received cholecalciferol and a 35-fold lower cumulative dose of 'active' vitamin D than that of Heidelberg and its coronary calcification prevalence was 10% instead of 92%, while their PTH suppression and demographic characteristics (with the exception of 2 years less on dialysis and 2 years more on transplantation) were comparable.

These observations should lead to systematic correction of vitamin D deficiency, even in dialysis patients, even though NKF-K/DOQI does recommend it only in chronic kidney disease (CKD) patients stage 3–4, but paradoxically not in ESRD patients in whom vitamin D deficiency is more severe.

1. 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.
2. Timms PM, Mannan N, Hitman GA *et al.* Circulating MMP9, vitamin D and variation in the TIMP-1 response with VDR genotype: mechanisms for inflammatory damage in chronic disorders? *QJM* 2002; **95**: 787–796.
3. Oh J, Wunsch R, Turzer M *et al.* Advanced coronary and carotid arteriopathy in young adults with childhood-onset chronic renal failure. *Circulation* 2002; **106**: 100–105.
4. Briese S, Wiesner S, Will JC *et al.* Arterial and cardiac disease in young adults with childhood-onset end-stage renal disease-impact of calcium and vitamin D therapy. *Nephrol Dial Transplant* 2006; **21**: 1906–1914.

JF Bonne[1], S Mailliez[1], M Assem Al Rifai[1], I Shahapuni[1], J Mansour[1] and A Fournier[1]
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Response to 'Osteodystrophy and dialysis survival'

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We appreciate the comments by Bonne *et al.*[1] The apparent mitigation of the survival advantage of higher doses of vitamin D was only observed with paricalcitol doses above 15 mcg/week.[2] Patients in the latter group had an average serum intact PTH concentration of 555 pg/ml, compared with 268 pg/ml in all other patients.[2] Hence, the weaker survival advantage in the high-dose paricalcitol group is not unlikely due to a high baseline PTH at the start of the cohort. Both we[2] and others[3] have shown that severe hyperparathyroidism is associated with increased death risk. Such excessive serum PTH concentrations usually lead to secondary administration of higher doses of vitamin D by nephrologists. The resultant 'selection bias by indication' may appear in the form of a spurious association between vitamin D dose and outcome. Nevertheless, it should be emphasized that in our study even patients who had received the highest paricalcitol dose

(>15 mg/week) exhibited significantly improved survival compared with those who did not receive paricalcitol during any calendar quarter.[2] Indeed, additional subgroup analyses have shown that the survival advantage of any dose of paricalcitol is robust and observed in all categories of maintenance dialysis patients irrespective of the serum concentration of calcium, phosphorus or PTH.[4] The latter data are consistent with subgroup analyses by Teng *et al.*,[5] who also showed survival advantages of every dose of vitamin D analog across diverse subgroups.

We agree with Bonne *et al.* that vitamin D deficiency may be an underappreciated problem in patients with chronic kidney disease and it is currently highly prevalent in dialysis patients.[6] However, regardless of the degree of vitamin D deficiency, therapy with paricalcitol was associated with better survival. Vitamin D deficiency may be associated with both inflammation and atherosclerosis.[7] Hence, administration of a 1-hydroxylated form of vitamin D appears advantageous both biologically and epidemiologically.

1. Bonne. Osteodystrophy and dialysis survival. *Kidney Int* 2007 in press.
2. 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.
3. Block GA, Klassen PS, Lazarus JM *et al.* Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. *J Am Soc Nephrol* 2004; **15**: 2208–2218.
4. Lee GH, Benner D, Regidor DL, Kalantar-Zadeh K. Impact of kidney bone disease and its management on survival of patients on dialysis. *J Ren Nutrition* 2007; **17**: 38–44.
5. 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.
6. Gonzalez EA, Sachdeva A, Oliver DA, Martin KJ. Vitamin D insufficiency and deficiency in chronic kidney disease. A single center observational study. *Am J Nephrol* 2004; **24**: 503–510.
7. Levin A, Li YC. Vitamin D and its analogues: do they protect against cardiovascular disease in patients with kidney disease? *Kidney Int* 2005; **68**: 1973–1981.

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