

# Effect of a Non-Calcium-Based Phosphate Binder on Fibroblast Growth Factor 23 in Chronic Kidney Disease

C. Spatz, K. Roe, E. Lehman, N. Verma

Nephron Clin Pract 2013;123:61-66  
 (DOI:10.1159/000351811)

## Commentary

By Professor Richard Glasscock

The bone-derived phosphatonin, Fibroblast Growth Factor-23 (FGF23), has attracted a great deal of attention in recent years. Almost 500 articles have been published on the subject (according to PubMed) in the last decade, and the pace of publication is accelerating. The primary areas of interest have been the role of FGF23 in bone and mineral metabolism, parathyroid hormone and endogenous calcitriol production in chronic kidney disease (CKD), but the broader effects of FGF-23 on other organ system, such as the heart, is also increasingly being investigated. Few studies have examined the effects of serum phosphorous reduction in CKD stages 3–5 by inhibition of intestinal absorption of phosphate (oral phosphate binding agents). Spatz and coworkers conducted a prospective cohort study of the effect of oral sevelamer carbonate (800 mg/day for 90 days) on serum FGF23 levels (C-terminal assay) in 40 hyperphosphatemic subjects with eGFR <60 ml/min/1.73 m<sup>2</sup> (average eGFR of 21.2 ± 10.5 ml/min/1.73 m<sup>2</sup>) not on dialysis therapy. Despite a significant but small lowering of the serum phosphorous level (4.8 ± 0.8 mg/dl to 4.4 ± 0.9mg/dl – an 8 % decrease), the serum FGF23 levels were unchanged (602 ± 1074RU/ml to 599 ± 721 RU/ml). Active Vitamin D therapy was kept constant during the period of observation. Immunoreactive PTH levels remained unchanged but 25-OH Vitamin D levels decreased slightly. Calcitriol levels were not measured.

While this essentially negative study adds to the literature on the subject, interpretations are limited by the short duration of observation, the small number of subjects examined (limiting the power of the study to detect real differences), the lack of monitoring of compliance, the wide variation in serum FGF23 levels at baseline, application of the C-terminal assay for FGF23 and the use of only one category of phosphate-binding agent. Also, one cannot be sure that phosphate absorption was affected because urinary phosphorous exposure was not monitored. It is unclear whether the serum samples were processed using K-EDTA, which can have an effect on intact FGF-23 stability [1].

In sum, although generally well-done, this study is inconclusive with respect to the impact of phosphorous lowering strategies on FGF23 levels. As of now, there are no demonstrable benefits of lowering of serum phosphorous levels in non-dialysis CKD, and the possibility of harm does exist [2]. Since FGF23 can be involved in the pathogenesis of left ventricular hypertrophy (LVH) in progressive CKD [3], resolution of this uncertainty is very important in the future. A proper randomized controlled study of intact and C-terminal FGF23 levels involving a large number of subjects with pre-dialysis CKD (normo- and hyper-phosphatemic) treated with calcium-containing and non-calcium-containing phosphorous binding agents using objective surrogate end-points such as LVH and vascular calcification is needed.

## References

- 1 Smith ER, Ford ML, Tomlinson LA, Weaving G, Rocks BF, Rajkumar C, Holt SG: Instability of fibroblast growth factor-23 (FGF-23): implications for clinical studies. *Clin Chim Acta* 2011;412:11–12.
- 2 Block GA, Wheeler DC, Persky MS, Kestenbaum B, Ketteler M, Spiegel DM, Allison MA, Asplin J, Smits G, Hoofnagle AN, Kooienga L, Thadhani R, Mannstadt M, Wolf M, Chertow GM: Effects of phosphate binders in moderate CKD. *J Am Soc Nephrol* 2012;23:1407–1415.
- 3 Faul C, Amaral AP, Oskouei B, Hu MC, Sloan A, Isakova T, Gutiérrez OM, Aguillon-Prada R, Lincoln J, Hare JM, Mundel P, Morales A, Scialla J, Fischer M, Soliman EZ, Chen J, Go AS, Rosas SE, Nessel L, Townsend RR, Feldman HI, St John Sutton M, Ojo A, Gadegbeku C, Di Marco GS, Reuter S, Kentrup D, Tiemann K, Brand M, Hill JA, Moe OW, Kuro-O M, Kusek JW, Keane MG, Wolf M: FGF23 induces left ventricular hypertrophy. *J Clin Invest* 2011;121:4393–4408.

[Follow and participate in the discussion of this article](#)