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MINERAL METABOLISM

High phosphate associated with renal disease progression

High phosphate level seems to be an independent risk factor for the progression of proteinuric chronic kidney disease (CKD), and might even reduce the renoprotective effect of angiotensin-converting-enzyme (ACE) inhibitors, say researchers in Italy.

> "These findings suggest that serum phosphate might be a specific target for renoprotective therapy in CKD patients..."

Findings from a number of observational studies have indicated that phosphate might be involved in the development and progression of CKD, but none of the analyses came from the setting of a clinical trial and no study had looked at the association between serum phosphate levels and renin–angiotensin system therapy, the current gold-standard therapy for the treatment of diabetic and nondiabetic progressive chronic nephropathies. Zoccali *et al.* therefore decided to investigate the associations between serum phosphate levels, progression of renal disease and treatment with the ACE inhibitor ramipril.

The investigators analyzed data from 331 of 352 patients involved in the REIN study, a prospective, randomized, placebo-controlled trial which showed that treatment with ramipril significantly reduced proteinuria in patients with chronic progressive nephropathies. Of the patients included in Zoccali *et al.*'s analysis, 165 had been randomly assigned to ramipril and 166 to placebo.

Over a median follow-up period of 30 months, four patients died, 74 patients progressed to end-stage renal disease (ESRD) and 10 patients had a doubling of serum creatinine level. Patients with serum phosphate levels in the highest two quartiles were significantly more likely to progress to ESRD or to have a doubling of serum creatinine level than were individuals with serum phosphate levels in the lower two quartiles (P <0.001).

In addition, the researchers found that increasing serum phosphate levels were associated with a progressive decrease in the protective effect of ramipril, an effect that persisted even after adjustment for potential confounding factors such as urinary protein level and glomerular filtration rate.

"These findings suggest that serum phosphate might be a specific target for renoprotective therapy in CKD patients and provide the background for randomized clinical trials to formally test whether reducing phosphate exposure by restricted dietary intake and/or concomitant treatment with phosphate binding agents may serve to optimize the renoprotective effect of ACE inhibition in this population," state the authors.

Rebecca Ireland

Original article Zoccali, C. *et al.* Phosphate may promote CKD progression and attenuate renoprotective effect of ACE inhibition. *J. Am. Soc. Nephrol.* http://dx.doi.org/10.1681/ASN.2011020175