Racial differences in parathyroid hormone levels in CKD

Tamara Isakova

Division of Nephrology and Hypertension, Department of Medicine, University of Miami, Miller School of Medicine, Miami, FL, USA

Correspondence and offprint requests to: Tamara Isakova; E-mail: tisakova@med.miami.edu

Patients with chronic kidney disease (CKD) are at increased risk for progressing to end-stage renal disease and developing cardiovascular disease [1]. Epidemiologic studies have demonstrated that abnormalities in mineral metabolism are independently associated with higher rates of these adverse outcomes [2, 3]. Moreover, the presence of mineral dysmetabolism is often used clinically as an indicator of chronicity and severity of kidney disease. Measurements of parathyroid hormone (PTH), serum phosphate, calcium and vitamin D levels are regularly obtained in the context of delivering clinical care to patients with CKD, and existing guidelines provide recommendations for target levels and triggers for initiation of therapy [4, 5]. However, randomized controlled trials evaluating the efficacy of the standard treatments on hard clinical endpoints are lacking, and marked within-person variability in these biochemical parameters exists.

Recent evidence has also suggested that there may be additional, between-person, variability in markers of mineral metabolism across subgroups of patients with CKD. Several reports have implicated race as an important factor that may influence PTH, serum phosphate and vitamin D levels [6, 7]. Briefly, these studies demonstrate that comparisons with whites, blacks have higher serum phosphate and lower urinary phosphate excretion despite higher levels of phosphaturic hormones, fibroblast growth factor 23 and PTH [6–9]. Calcitriol levels are also higher in blacks, despite lower 25-hydroxyvitamin D levels [6, 10]. In this issue of the Nephrol Dial Transplant, a cross-sectional analysis of laboratory data from 2028 patients with CKD (505 black) provides additional information to consider [11].

Ennis et al. set out to investigate the differences in PTH levels by race and aimed to examine the independent contribution of the estimated glomerular filtration rate (eGFR), serum calcium, phosphate and 25-hydroxyvitamin D in relation to these differences. The authors used laboratory and minimal demographic and clinical data available from a laboratory-based CKD service. In unadjusted analysis, the authors found that starting at CKD stage 2 and through CKD stage 5, PTH levels were significantly higher in blacks compared with whites. In contrast to prior studies, there were no significant differences by race in serum phosphate at any CKD stage. 25-Hydroxyvitamin D levels were lower in blacks at stages 1–3. In the adjusted models, the top three determinants of PTH level were eGFR, 25-hydroxyvitamin D level and black race. Moreover, there was a significant interaction between eGFR and black race on the PTH level, indicating that the slope of the rise of PTH as a function of declining eGFR was steeper in blacks versus whites. Interestingly, the other parameters considered in multivariable models contributed minimally to the PTH level and only had additive but not multiplicative effects (no significant interaction between serum phosphate and race, or between 25-hydroxyvitamin D and race, on PTH level). Finally, the authors reported that all the variables together accounted for only 42% of the variation in the PTH level. This suggests that additional unmeasured factors, previously reported to associate with PTH level (smoking, body mass index, dietary calcium and phosphate intake, medications) [12–14], if available, could have improved the predictive ability of the adjusted model.

Despite the potential for residual confounding, the results from the study by Ennis et al. [11] confirm the observations from prior reports and once again highlight the existence of racial differences in mineral metabolism in CKD. The finding of a steeper slope of the relationship between PTH and eGFR in blacks compared with whites that was not explained by the changes in serum phosphate, calcium and 25-hydroxyvitamin D points to potential novel and, perhaps, as of yet undiscovered or poorly described mechanisms for these differences. For example, racial differences in bone turnover [15] and skeletal responsiveness to PTH may play a role in the observed biochemical phenotype. Alternatively, racial differences in sensitivity to phosphaturic effects of PTH and fibroblast growth factor 23 at the level of the kidney may have an effect on the circulating levels of these hormones. Environmental factors, such as income [16], dietary intake of foods rich in phosphate additives and access to care, may also contribute. Finally, ancestry-based genetic differences may underlie racial differences in mineral metabolism in health and in CKD. Each of these requires dedicated inquiry, and the findings may help identify novel therapeutic targets.

Blacks with CKD are at greater risk for cardiovascular disease and end-stage renal disease compared with whites [17, 18]. Racial differences in mineral metabolism may mediate some of the excess risk. In the case of PTH, the available observational data on its association with clinical outcomes in all-comers with CKD are less convincing...
compared with other markers of mineral metabolism [3, 19]. Though a racial difference in bone biopsy findings exists in patients on dialysis [15], minimal comparable data are available in earlier stages of CKD. Thus, the existing evidence is insufficient to support a change in guidelines, as Ennis et al. conclude. Instead, these and similar findings should prompt additional efforts to clear up the existing uncertainties.

Acknowledgements. T.I. was supported by grant K23DK087858 from the National Institutes of Health.

Conflict of interest statement. None declared.

(See related article by Ennis et al. Contribution of calcium, phosphorus and 25-hydroxyvitamin D to the excessive severity of secondary hyperparathyroidism in African-Americans with CKD. Nephrol Dial Transplant 2012; 27: 2847–2853.)

References


Received for publication: 19.3.2012; Accepted in revised form: 1.4.2012