Response to ‘Targeting hyperphosphatemia: truth or dare’

We thank Meijers and Evenepoel1 for their comments in ‘Targeting hyperphosphatemia: truth or dare.’ We agree that the most desirable study of phosphorus binders on dialysis is a blinded, placebo-controlled randomized trial. We also agree that challenging existing paradigms is essential, especially when those paradigms themselves are based largely on expert opinion, as in the case for serum phosphate targets on dialysis. Unfortunately, however, practical considerations must often prevail over ideal theory to force compromises in the interest of progress. In our opinion, the use of phosphorus binders on dialysis is one example where such concessions may need to be made. We would eagerly support and participate in a double-blinded placebo-controlled study if it was proven that recruitment and retention of participants was feasible in the real world. We are skeptical, however, given the widespread view among nephrologists that control of phosphate is the most important aspect of the management of mineral metabolism on dialysis. This attitude would lead to preferential withdrawal of participants from the placebo arm in the event of severe hyperphosphatemia. With limited research resources and numerous questions to be answered, the risk of failure of the ‘perfect’ phosphorus binder study on dialysis due to poor enrollment, limited power, and bias would be unacceptably high. At the crossroads of theory and practice, we believe that a trial of more- versus less-intensive phosphate control will present a far greater chance for operational success and will yield critically important results that would be readily transferable into practice. Regardless of how the nephrology community ultimately proceeds, we are excited that our blueprint has initiated a much-required dialogue exemplified by the comments made by Meijers and Evenepoel.
Response to ‘The case of the solitary sick kidney’


In their letter regarding my editorial, ‘When is one kidney not enough?’1 Stratta et al2 argue that mutations of HNF-1β should be considered as an etiology for unilateral renal agenesis, and that genetic screening should be included in the evaluation of such patients. Mice heterozygous for a mutation leading to a deficiency in another transcription factor, SIX2, also exhibit severe renal maldevelopment, with marked renal hypoplasia and reduced nephron number.3 In addition to HNF-1β and SIX2, there are a number of genes contributing to renal morphogenesis, some with more subtle phenotypic expression. These include variants of the RET and PAX2 alleles, each of which may result in renal hypoplasia.4,5 Importantly, the combination of hypomorphic RET and PAX2 alleles has an additive effect in reducing the kidney volume (a proxy for nephron number) in human neonates.5 Continued elucidation of the molecular control of renal morphogenesis will reveal more genes responsible for both congenital renal anomalies and progression of renal insufficiency. Once the temporal expression and relative contribution of individual genes in the developing kidney are better understood, the relative risk for progression can be assigned. As pointed out by Stratta et al, such genetic screening could be added to the development of biomarkers of progression and monitoring risk factors already identified.


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