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RESEARCH perspectives

Chronic Kidney Disease-Mineral and Bone Disorder: Translating Evidence Into Practice

Dear Colleague:

Kidney disease is a pandemic associated with high mortality rates. The high number of chronic kidney disease (CKD) patients poses a challenge for nephrologists and primary care physicians, especially when managing the combination of secondary hyperparathyroidism and mineral bone disease. This CME-certified activity, *Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD): Translating Evidence Into Practice,* highlights current research on the pathogenesis of CKD-MBD, and assesses the clinical implications of recent data and ongoing trials involving various classes of phosphate binders, noncalcium phosphate binders, calcimimetics, and other agents, for the treatment of secondary hyperparathyroidism, to incorporate into your clinical practice.

A large review of calcium-based binders and a noncalcium phosphate binder shows the impact of agents on cardiovascular calcification and mortality risk in patients with CKD-MBD.

- This meta-analysis showed a significant difference in coronary artery calcification scores (CACS) and aortic calcification scores (ACS), and suggests sevelamer, a phosphate binding agent, benefits dialysis patients in terms of CACS, ACS, and hypercalcemia.
- Compared with calcium-based phosphate binders, sevelamer therapy resulted in smaller decreases in serum levels of phosphorus and a lower prevalence of hypercalcemia.
- Studies also show the use of sevelamer can result in a reduction in hospitalization.

Ref. Wang C, Liu X, Zhou Y, et al. *PLOS ONE.* 2015;10:e0133938.

Novel agents have been shown to improve secondary hyperparathyroidism.

- Etelcalcetide is an injectable calcimimetic with a longer elimination half-life than cinacalcet; it may also improve adherence and reduce pill burden.
- Clinical trials have demonstrated etelcalcetide to be more effective than cinacalcet in lowering PTH concentrations and managing secondary hyperparathyroidism in hemodialysis patients.

Refs. Block GA, et al. *JAMA*. 2017;317:156-164; Block GA, et al. *JAMA*. 2017;317:146-155.

In the recent clinical trial by Sprague and colleagues, extended-release caldifediol provides a promising alternative treatment for secondary hyperparathyroidism.

- Vitamin D deficiency is shown through calcitriol deficiency decreasing intestinal calcium absorption, leading to hypocalcemia and diminished tissue levels of vitamin D receptors, which results in resistance to calcitriol-mediated regulation and stimulation of PTH secretion leading to secondary hyperparathyroidism.
- The Sprague, et al, study shows ER calcifediol may provide a more reliable and standardized approach to vitamin D repletion than commonly used regimens of nutritional vitamin D in patients with stage 3 or 4 CKD.

Ref. Sprague SM, et al. *Am J Nephrol.* 2016;44:316-325.

The iron contained in ferric citrate has been show to provide exogenous iron and may lessen the

requirement for erythropoietin.

- Studies show ferric citrate effectively decreased serum phosphorus levels, with similar effects on other markers of bone and mineral metabolism as active control in hemodialysis and peritoneal dialysis patients.
- There is a need for better and more effective phosphate binders.

Ref. Van Buren PN, Lewis JB, Dwyer JP, et al. *Am J Kidney Dis.* 2015;66(3):479-488.

Addressing the clinical gaps from 2009 KDOQI and KDIGO guidelines:

- Clinical practice gaps with the use of the KDOQI and KDIGO global guidelines, and local clinical practices in CKD-MBD, may result because implementation on local levels is not always applicable, due to medical care and social factors.
- An attempt is made to address this gap through updates to the 2009 KDIGO guidelines, with the aim to align recent studies with more current standard of care in clinical practice. Please find an executive summary outlining specific updates to the KDIGO guidelines, and why they matter, as posted (July 2017) in *Kidney Int.*

http://www.kidney-international.org/article/S0085-2538(17)30249-1/fulltext .

Clinicians need an improved understanding of the mechanisms underlying CDK-MDB to identify the disease and make informed treatment decisions. Our review of recent studies involving various classes of phosphate binders, and other agents for the treatment of secondary hyperparathyroidism, show the potential impact on the management of patients with CKD-MBD in your practice.

Yours sincerely,

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