Mineral and Bone Disorders in CKD – New KDIGO Update

What’s the latest evidence affecting clinical management of mineral and bone disorder in chronic kidney disease? Updated recommendations by the Kidney Disease: Improving Global Outcomes (KDIGO) Global Network are now available.

The 2017 KDIGO Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD) guideline update has implications for diagnosis, evaluation, prevention, and treatment of secondary CKD-MBD in children and adults. The full guideline has been published as a supplement to *Kidney International*; an Executive Summary appears in the July issue of *Kidney International*.

Updating the previous guideline published in 2009, the revision reflects new research related to management of CKD-MBD. In a key change, it recommends against routine use of calcitriol or vitamin D analogs for treatment of abnormal parathyroid hormone (PTH) levels.

That change reflects a continued lack of data on the optimal PTH level for patients with CKD G3a to G5. Meanwhile, the 2017 Update Working Group believes that maintaining PTH may be an “appropriate adaptive response” to decreased kidney function.

“Randomized controlled trials have not really shown a benefit and perhaps harm because of hypercalcemia,” said Michael J. Germain, MD, Professor of Medicine, Tufts University School of Medicine and Nephrologist/Partner, Western New England Renal & Transplant Associates, PC, Springfield, Mass. Calcitriol and vitamin D analogs “do a good job in terms of suppressing PTH, but they haven’t shown a benefit in terms of other outcomes, including cardiovascular outcomes.”

The update suggests that calcitriol and vitamin D analogs “not be routinely used” in adults with CKD G3a-G5 not on dialysis. Although there was no “uni-form consensus” regarding this recommendation, it reflects a lack of data showing benefits of these older drugs on patient-level outcomes.

The revised guideline mentions a potential new alternative for secondary hyperparathyroidism. Extended-release (ER) calcifediol (Rayaldee) was recently approved for use in adults with stage 3 or 4 CKD and serum total 25-hydroxyvitamin D less than 30 ng/mL. Approval was based on trials showing that ER calcifediol reduced intact PTH while increasing 25D. Effects proved for use in dialysis patients earlier this year.

An updated recommendation states that it’s “reasonable” to reserve calcitriol and vitamin D analogs for patients with CKD G4-G5 with severe progressive hyperparathyroidism. In children, these drugs “may be considered” to maintain serum calcium in the normal range for age.

Other revised recommendations address:

**CKD-MBD Diagnosis.** Recent studies have added evidence that measuring bone mineral density (BMD) predicts fractures in patients with CKD, as in the general population. On that basis, BMD assessment is suggested to assess fracture risk in CKD G3a-G5D, if the results will affect treatment decisions.

Bone biopsy is considered “reasonable” if information on the type of renal osteodystrophy will affect treatment. Dr. Germain cites that recommendation as an example of how guidelines based on literature reviews may provide limited guidance for nephrologists in practice. “The problem is that very few people can get biopsies” due to the lack of specialized pathology personnel and equipment. “If [KDIGO] are going to recommend [bone biopsy], they really have to acknowledge the fact that it’s impossible to get for probably 95% to 99% of nephrologists.”

**Serum phosphate and calcium.** Recent studies have linked higher serum phosphate levels to increased mortality, but there’s still a lack of evidence that phosphate-lowering therapy improves patient outcomes. The revised guideline removes a previous recommendation to maintain phosphate in normal range, instead focusing on treatment for hyperphosphatemia. It also discusses new data on calcium-containing versus calcium-free phosphate binders.

**Antiresorptive and other osteoporosis therapies.** Recommendations for antiresorptive and other osteoporosis treatments were broadened from CKD G3a-G5b to G3a-G5d. Treatment choices should consider specific side effects and the accuracy of the underlying diagnosis.

**Kidney transplant bone disease.** The update addresses the use of BMD testing to assess fracture risk. Evidence supports treatment suggestions for the first 12 months, but not thereafter.

The KDIGO Working Group notes that its updated guideline still reflects a “dearth of high-quality evidence…in several areas pertaining to CKD-MBD.” Research priorities “need to be very focused on the patient’s experience,” Dr. Germain believes. “I would concentrate more on bone health and what the patient experiences, so they feel better.” He thinks that nephrologists treating MBD need to “know a little bit more about what the patient’s symptoms are in dialysis and what could be related to the hyperparathyroidism.”

“And then, does treatment actually improve their symptoms and their day-to-day life?” He emphasizes the need for studies focusing on patient-reported outcomes and giving patients more choices and input into treatment decisions—notably including choices about phosphate binder therapy.

**Suggested Reading**


### Findings

**In Black Patients with Type 1 Diabetes, Hba1c Underestimates Mean Glucose**

Glycated hemoglobin (HbA1c) levels may underestimate mean glucose level in African Americans with type 1 diabetes, reports a study in *Annals of Internal Medicine*.

The T1D Exchange Racial Differences Study Group analyzed data on 104 non-Hispanic black and 104 non-Hispanic white patients with type 1 diabetes, enrolled at 10 US centers. (Individuals with anemia or hemoglobinopathy were excluded.) All subjects were at least 8 years old and had type 1 diabetes for at least 2 years. Mean glucose concentration was measured by continuous glucose monitoring, and racial differences in the relationship between glucose and HbA1c were assessed.

In this population with type 1 diabetes, mean HbA1c was 9.1% in black subjects compared to 8.3% in white subjects; mean glucose concentration was 191 versus 180 mg/dL, respectively. At a given mean glucose concentration, HbA1c was 0.4 percentage point higher in blacks compared to whites. The results were similar on analysis of subjects with a higher number of continuous glucose monitoring measurements.

The racial difference in mean glucose-HbA1c relationship also persisted on stratified analysis by age under 18 years versus age 18 or older. Glycated hemoglobin and fructosamine were highly correlated with HbA1c, with no clinically significant difference by race.

Studies have consistently reported higher HbA1c levels in black compared to white adults and children with type 1 or 2 diabetes. Although this could indicate poorer glycemic control in black patients, it might also reflect racial differences in glycation of hemoglobin.

This study suggests that HbA1c overestimates mean glucose concentration in black patients with type 1 diabetes. While this could reflect racial differences in, hemoglobin glycation, race only partly explains the observed difference in HbA1c. The authors write, “Future research should focus on identifying and modifying barriers impeding improved glycemic control in black persons with diabetes” [Bergenstal RM, et al. Racial differences in the relationship of glucose concentrations and hemoglobin A1c levels. *Ann Intern Med* 2017; doi:10.7326/M16-2596].