Developed by: ANNA Specialty Practice Networks

Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Fact Sheet

Overview

Chronic kidney disease-mineral and bone disorder (CKD-MBD) is a systemic disorder of mineral and bone metabolism due to CKD manifested by either one or a combination of the following:

(i) Abnormalities of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D metabolism.
(ii) Abnormalities in bone turnover, mineralization, volume, linear growth, or strength.
(iii) Vascular or other soft tissue calcification. (KDIGO, 2017)

As kidney function declines, there is a progressive deterioration in mineral homeostasis. Disorders of mineral metabolism and bone disease are common complications in patients with CKD and are associated with increased morbidity and mortality as well as decreased quality of life (QoL) (Brown & Gilliland, 2020).

These disorders lead to a constellation of bone lesions which was previously referred to as renal osteodystrophy (ROD), with affected patients manifesting with symptoms such as bone pain, muscle-tendon rupture, pruritus, and high incidence of fractures. *ROD* is the bone component of CKD-MBD and is defined as alterations in bone morphology associated with progressive CKD (Khan, 2018).

Disorders of bone and mineral metabolism are independently related to mortality and morbidity associated with cardiovascular disease and fractures in patients on hemodialysis (HD) or peritoneal dialysis (PD) (Iseri et al., 2020); Slouma et al., 2020).

Disease Manifestation and Possible Symptoms

Clinical Progression of Mineral and Bone Disorder (MBD) in CKD

- Phosphorus excretion diminishes, leading to an increase in serum phosphorus.
- Calcium is not reabsorbed, leading to decreased serum calcium.
- Vitamin D is not activated, leading to hypertrophy and hyperplasia of the parathyroid glands with increased secretion of PTH.
- Both decreased serum calcium levels and increased serum phosphorus levels stimulate excessive secretion of PTH.
- Abnormalities in bone turnover and mineralization.
- Vascular and other soft tissue calcification.

An elevated PTH increases both the number and activity of osteoclasts (cells that break down bone). As osteoclasts break down bone, calcium and phosphorus are released into the serum, causing an elevation in phosphorus levels. This leads to demineralized (weakened) bones, which are subject to fractures; falls; and calcification of the heart, vasculature, and soft tissues.

The disease process occurs as renal function decreases to a GFR less than 60 mL/min/1.73m^2:

- Decreased urinary phosphorous excretion.
- Decreased vitamin 1,25 D levels due to the kidney's inability to convert 25 D into the biologically active form.
- Increased PTH secretion as a response to stimulate calcium absorption in the intestines.
- Decreased calcium excretion.

CKD progression into G3 - G4, induces serum changes:

- Phosphorus increases.
- PTH increases.
- Calcium imbalance (decreases) due to decreases in vitamin 1,25 D.
- Fibroblast growth factor 23 (FGF23) increases to compensate for phosphate retention.

This condition may be present and undetected for a long period of time prior to the initiation of kidney replacement therapy (KRT). If left uncontrolled, clinical evidence has demonstrated an increase in mortality in patients with CKD (Waziri et al., 2019).

The clinical manifestations may include (Brown & Gilliland, 2020):

- Bone pain and/or risk for fractures.
- Muscle weakness.
- Exacerbated hyperphosphatemia.
  - Secondary hyperparathyroidism (results from retained phosphorus, low levels of vitamin D, and a reduction in serum calcium).
- Risk for calcium overload.

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- Itching (due to increased phosphorous or PTH levels).
- Coronary and peripheral vascular calcification.
- Reddened eyes (due to capillary deposition of minerals).
- Calcifications of the skin, muscles, and subcutaneous tissues.

Diagnostic Testing

For patients on HD or PD, the following should be maintained at the designated level (Isakova et al., 2017).

CKD Stage 5, Patients on Dialysis

- Serum phosphorus (PO_4): 3.5 to 5.5 mg/dL.
- Serum calcium (Ca): 8.4 to 9.5 mg/dL.
- Calcium/phosphorus ($CaPO_4$) Product: less than 55 mg^2/dL^2.
- PTH: 150 to 300 pg/mL.

Clinical Practice Guidelines

The following clinical practice guidelines were recommended based on clinical evidence review (KDIGO, 2013).

Stage 3 (GFR 30 to 59 mL/min/1.73m²)

- PTH: Greater than the upper limit of normal for the assay used.
- Phosphorous: Within normal limit.
- Calcium: Within normal limit.

Stage 4/5 (GFR 15 to 29 mL/min/1.73m²)

- PTH: Greater than the upper limit of normal for the assay used.
- Phosphorous: Maintain normal.
- Calcium: Maintain normal.

Stage 5D (or on Replacement Therapy [RRT])

- PTH: 2 to 9 times the upper limit of normal for the assay used.
- Phosphorous: Treat toward normal.
- Calcium: Maintain normal.

Other Laboratory Tests that May Be Useful for All Stages

- Alkaline phosphatase: 20 to 140 international units/L.
- CO_2: Greater than 22 mEq/L.
- Aluminum levels: Less than 20 mcg/L.
- Vitamin D levels (rarely measured).

Other Diagnostic Testing that May Be Useful

- Bone X-rays for suspected fractures.
- Bone biopsy from the iliac crest.
- Dual imagery X-ray absorptiometry (DXA) to visualize bone lesions.
- Radiographs to detect possible calcifications.
- Electrocardiogram and echocardiogram.

Complications of Mineral Imbalance

Vascular Complications

- Cardiovascular problems resulting in arteriosclerosis, vascular calcification, valvular calcification, and cardiomyopathy.
- Progressing cardiovascular disease may, in turn, lead to cardiovascular problems, such as myocardial infarction, peripheral vascular disease (which presents as calciphylaxis and ulcers in the torso and extremities), and cerebrovascular disease in the form of transient ischemic attacks and cerebrovascular accidents.

Osteodystrophy (Bone Disease) Complications

- Determined by bone biopsy and estimated with monitoring of serum levels.
- High turnover bone diseases:
  - Mixed uremic osteodystrophy with varying degrees of mineralization defects and hyperparathyroid changes.
  - Osteitis fibrosa is an abnormal bone reabsorption, formation, and marrow fibrosis.
- Low turnover bone diseases:
  - Adynamic bone disease suppresses bone formation secondary to hypercalcemia and/or over suppression of PTH.
  - Osteomalacia produces large amounts of unmineralized bone, and it may be aluminum- or nonaluminum-related. Osteomalacia has decreased substantially because aluminum binder use has diminished.

Interventions

Interventions to prevent and treat disorders of bone/mineral metabolism include diet, medications, and dialysis. The patient may require surgical intervention if these interventions are not successful.

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Diet

Due to a high need for protein consumption, it is virtually impossible to eat a phosphorus-free diet; therefore, phosphorus is restricted, and phosphate binders must be used. Patients should also be instructed to check food labels for potassium, calcium, or phosphorus, which may impact their overall health.

Isakova and colleagues (2017) suggest the following guidelines for daily mineral intake:

- Phosphorus: 800 to 1,000 mg/day.
- Calcium: 1,000 to 1,200 mg/day from all sources (including phosphate binders).

High-phosphorus foods that should be restricted include (Ignativicius et al., 2021); National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK], 2016):

- Dairy products
- Dark cola.
- Dried beans.
- Whole grains.
- Nuts.
- Baked goods made from a mix.
- Chocolate.
- Foods containing phosphorus additives.
- Processed meats.

Medications

Phosphate Binders

Phosphate binders work by binding phosphorus in the digestive system, beginning in the small intestine and eliminated in the stool. It is imperative binders be administered with food or as per the package insert. Phosphate binders should not be administered with any other medications. Adherence to prescribed regimens is crucial.

Phosphate binders are a commonly prescribed class of drug for patients with renal disease and account for up to 50% of the daily pill burden in patients with CKD. The frequent adverse drug effects (particularly gastrointestinal intolerance) contribute to poor medication adherence. Therefore, patients should be screened for any underlying gastrointestinal pathology prior to administration of any phosphate binder (Chan et al., 2017).

According to Isakova and colleagues (2017), the following recommendations are stated in the KDOQI and KDIGO guidelines regarding the discontinuation of calcium-based binders in patients with CKD in the presence of:

- Serum calcium greater than 10.2 mg/dL[2] (KDOQI).
- PTH less than 150 pg/mL[2] (KDOQI).
- Signs of calcification on radiographs or other diagnostic reports (KDIGO).

Calcium-Based Binders

Calcium carbonate (Tums®, Tums® EX), calcium acetate (Phoslo®), and calcium citrate (Citracal®).

Non-Calcium, Non-Metal-Based Binders

Sevelamer hydrochloride (Renagel®) (Sanofi, 2021a) and sevelamer carbonate (Renvela®) (Sanofi, 2021b).

Metal-Based Binders

Lanthanum carbonate (Fosrenol®) and aluminum (Alucaps®, Alternagel®, and Basogel®).

- Due to concerns of potential neurological toxicity, it is recommended to avoid or restrict the use of aluminum binders and to advocate for the use of newer binders (KDIGO, 2017).

Magnesium-Based Binders

- MagneBind®:
  - Requires monitoring of magnesium levels and contains calcium as well (National Kidney Foundation [NKF], 2019).

Vitamin D Analogs

Vitamin D analogs are used to suppress parathyroid production and secretion and to treat hypocalcemia.

- Calcijex® (calcitriol injection):
  - Reduction of PTH has been shown to result in an improvement in renal osteodystrophy (Abbott Laboratories, 2017).
- Rocaltrol® (calcitriol capsules and oral solution):
  - Pre-dialysis patients: Rocaltrol is indicated in the management of secondary hyperparathyroidism and resultant metabolic bone disease in patients with moderate to severe chronic renal failure (CCr 15 to 55 mL/min) mL/m[2] not yet on dialysis for hyperparathyroidism.
  - Patients on dialysis: Rocaltrol is indicated in the management of hypocalcemia and the resultant metabolic bone disease in patients undergoing chronic renal dialysis.

  - Patients with hypoparathyroidism: Rocaltrol is also indicated in the management of hypocalcemia and its clinical manifestations in patients with post-surgical hypoparathyroidism, idiopathic hypoparathyroidism, and pseudohypoparathyroidism (Validus Pharmaceuticals, 2018).
- Hectorol® (doxercalciferol injection):
  - Hectorol is indicated for the treatment of secondary hyperparathyroidism in patients with CKD on dialysis (Sanofi, 2018).
- Hectorol® (doxercalciferol capsules):
  - Patients on dialysis: Hectorol is indicated for the treatment of secondary hyperparathyroidism in patients with CKD on dialysis.
  - Pre-dialysis patients: Hectorol is indicated for the treatment of secondary hyperparathyroidism in patients with CKD Stage 3 or Stage 4 (Sanofi, 2018).
- Zemplar® (paricalcitol injection):
  - Zemplar is indicated for the prevention and treatment of secondary hyperparathyroidism associated with CKD Stage 5 (AbbVie Inc., 2021a, 2021b).
- Zemplar® (paricalcitol capsules):
  - Pre-dialysis patients: Zemplar is indicated for the prevention and treatment of secondary hyperparathyroidism associated with CKD Stages 3 and 4 (AbbVie Inc., 2021a, 2021b).

Calcimimetic Agents (Cinacalcet [Sensipar®])
Indicated for the treatment of secondary hyperparathyroidism in patients with CKD on dialysis and for the treatment of hypercalcemia in patients with parathyroid carcinoma. It increases the sensitivity of the calcium-sensing receptors on the parathyroid gland to calcium. Available in tablets (Amgen Inc., 2019).

Dialysis (Hemodialysis and Peritoneal Dialysis)

Dialysate is phosphorus-free to remove the maximum amount of phosphorus. If phosphorus remains elevated, longer or more frequent dialysis may be recommended. The recommended dialysate calcium concentration is 2.5 mg/dL with tailoring to individual patients as needed (NKF, 2019).

Parathyroidectomy

Recommended in patients with severe hyperparathyroidism (iPTH persistently greater than 800 pg/mL) with hypercalcemia and hyperphosphatemia, and non-responsive to medical therapy.

Implications for Nephrology Nursing

The registered nurse needs to assess, educate (importance of diet and compliance of medications), and monitor laboratory values to prevent the progression of metabolic bone disease. The advanced practice registered nurse needs to assess and intervene as follows (Campoy, 2020).

Assessment

- Monitor and interpret laboratory results and diagnostic studies and adjust medications as needed.
- Monitor the patient's ability and response to the treatment plan (i.e., dietary modifications, taking phosphate binders, taking calcium and vitamin D supplements).
- Monitor any development of bone disorders (i.e., calcifications and bone fractures).

Intervention

- Treat disorders of CKD-MBD following evidence-based research and guidelines.
- Order additional laboratory and diagnostic studies as appropriate (i.e., X-ray, bone scan, echocardiogram).
- Adjust diet and medication regimen as indicated based on biochemical parameters and patient response to therapy explaining the importance of the modifications to the patient.
- Refer patients with severe CKD-MBD for bone biopsy and additional bone treatment when warranted (i.e., unexplained fractures, unexplained bone pain, unexplained hypophosphatemia, and possible aluminum toxicity).

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ANNA Mission Statement

ANNA improves members' lives through education, advocacy, networking, and science.

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