CKD: Bone Mineral Metabolism

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HAPPY NEW YEAR

I MADE YOU A SANDWICH
CKD - KDIGO

Definition and Classification of CKD

- CKD: abnormalities of kidney structure/function for > 3 months with health implications
  - ≥1 marker of kidney damage:
    - ACR ≥30 mg/g
    - Urine sediment abnormalities
    - Electrolyte and other abnormalities due to tubular disorders
    - Abnormalities detected by histology
    - Structural abnormalities (imaging)
    - History of kidney transplant

- OR GFR < 60
Parathyroid glands

- 4 glands behind thyroid in front of neck
Parathyroid physiology
Parathyroid hormone

- Normal circumstances PTH:
  - Increases calcium
  - Lowers PO4 (the renal excretion outweighs the bone release and gut absorption)
  - Increases Vitamin D

- Controlled by feedback
  - Low Ca and high PO4 increase PTH
  - High Ca and low PO4 decrease PTH
In renal disease: Gets all messed up!

- Decreased phosphate clearance: **High Po4**
- Low 1,25 OH vitamin D = **Low Ca**
- Phosphate binds calcium = **Low Ca**
- Low calcium, high phosphate, and low VitD all feedback to cause **more PTH release**

- This is referred to as **secondary hyperparathyroidism**
- Usually not seen until GFR < 45
Who cares

• Chronically high PTH
  ◦ High bone turnover = renal osteodystrophy
    • Osteoporosis/fractures
    • Osteomalacia
    • Osteitis fibrosa cystica

• High phosphate
  ◦ Associated with faster progression CKD
  ◦ Associated with higher mortality

• Calcium-phosphate precipitation
  ◦ Soft tissue, blood vessels (eg: coronary arteries)

• Low 1,25 OH-VitD
  ◦ Immune status, cardiac health?
KDIGO

- KDIGO: Kidney Disease Improving Global Outcomes
- Most recent update regarding “Mineral and bone disorders” was 2017, previous guidelines were in 2009
So what can we do? KDIGO

- Monitor serum Ca, PO4, PTH, ALP at least once once GFR < 60 (Stage 3a)
- Frequency of measurement depends on CKD stage (q1-6 months)
Phosphate

- KDIGO 2017: “Suggest lowering phosphate towards the normal range”
- Practically we tend to target PO4 level of 1.1 – 1.8 mmol/L in patients with very low GFR
Phosphate

- DIET!!!
- Phosphate binders
  - Calcium based 1st line (cheaper)
    - Calcium carbonate or Calcium acetate
    - Max 1.5 g/day elemental calcium
    - Acetate lower calcium load
  - Non-calcium based ($), 2nd line
    - Use when hypercalcemic or calcium load too high
    - Evidence of reduced coronary calcification
    - Sevelamer (renagel)
    - Lanthinum ?safety
    - KIDGO recommends avoiding aluminum containing binders
Calcium

- Guidelines basically suggest avoiding hypercalcemia
- Avoid high doses of calcium binders
PTH

- The optimal level of PTH is not clear in CKD
- Treat reversible causes (low Ca, high PO4) in progressively rising PTH
- In CKD5 we generally target level 2-9x the upper limit of normal (Normal =8-9 pmol/L)
  - Based on CSN 2006 guidelines
- CKD patients should have a higher “expected PTH”
- Basically want to avoid having it too high or too low (both can cause problems)
PTH

- First line: Treatment of high PO4 and low Calcium
- If still high, add activated vitamin D
  - Alfacalcidol (one-alpha)
  - Calcitriol (if liver failure)
- Can use cinacalcet or parathyroidectomy in difficult to control disease (this typically occurs in end stage renal disease)
Vitamin D

Solar UVB radiation (290-320 nm)

7-Dehydrocholesterol → Cholecalciferol (vitamin D-3)

Secondary source from food/supplements
- vitamin D-3 (fish, meat); vitamin D-2 (mushrooms)

25-Hydroxyvitamin D [25(OH)D]

25-hydroxyvitamin D-1α-hydroxylase

1,25 di-hydroxyvitamin D [1,25(OH)₂D]

Conversion of 25(OH)D to 1,25(OH)₂D in the kidney is tightly regulated by PTH, calcium, and phosphorus levels
Some other tidbits
Primary hyperparathyroidism

- Parathyroid adenoma or hyperplasia
Primary hyperparathyroidism

- Parathyroid adenoma causes excess PTH secretion
- Not responsive to negative feedback
- High PTH, High Calcium, Low phosphate
- Different from secondary in renal failure where you get high phosphate and low calcium
- Requires surgical intervention
Primary hyperparathyroidism

- We do see this in our CKD patients and catching it is important.
- Some clues: PTH higher than expected for level of GFR, calcium high, phosphate low.
Tertiary hyperparathyroidism

- In the setting of renal failure and prolonged secondary hyperparathyroidism
- Chronic stimulation of parathyroid gland leads to hyperplasia, and autologous PTH secretion
- +++ PTH, High Ca, High PO4
- Severe bone disease
- Needs surgery
- Sometimes can be medically managed (cinacalcet)
Questions??