MULTIDISCIPLINARY DISCUSSION TOOL

Mineral Bone Disease Management
Stage 5 CKD / Dialysis

BC Renal Agency
An agency of the Provincial Health Services Authority

Optimum targets and treatment approaches to management of calcium, phosphorus and parathyroid hormone levels in end stage kidney disease have not been established. Several targets have been proposed and are listed in the following table:

Target	Serum Calcium	Serum Phosphate	iPTH
CSN 2006 Hemodialysis	Normal range 2.2 – 2.6 mmol/L	Normal range 0.78 – 1.53 mmol/L	10.6 - 53 pmol/L
KDOQI 2003 Hemodialysis	Low normal range 2.2 – 2.4 mmol/L	1.1 – 1.8 mmol/L	16.5- 33 pmol/L
KDIGO 2009	Avoid hypercalcemia Unknown if risk associated with moderate degree of hypocalcemia.	Lower elevated levels towards normal range	2-9 x upper limit of normal 14-63 pmol/L

- Treatment goals should be selected for each patient based on individual comorbidities, long-term benefits expected from control, adherence issues and quality of life.
- Increased dialysis dose may be the most effective treatment for elevated phosphorus.
- Prescription of non-calcium based phosphorus binders (aluminum hydroxide, lanthanum, niacin, sevelamer) should be reviewed and use of calcium based binders reconsidered when patient is no longer hypercalcemic.
- The following tool (see page 2) was created to assist the patient care team with discussions concerning phosphate management in patients on dialysis.

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SERUM PHOSPHATE GREATER THAN SELECTED TARGET RANGE

Follow trends—one high result does not indicate the need for change

Review dietary phosphorus intake, phosphorus binder use, dialysis dose and dialyzer prescription

SERUM CALCIUM LESS THAN TARGET

TREAT SYMPTOMATIC HYPOCALCEMIA:*
Consider oral calcium, dialysate calcium, vitamin D analogue

If not symptomatic

1. Stop non-calcium based binders and start or increase calcium-based binders.

2. <u>iPTH less than selected target</u>
   - Maintain or reduce vitamin D analogue

   <u>iPTH in selected target range</u>
   - Maintain vitamin D analogue

   <u>iPTH greater than selected target</u>
   - Start or increase vitamin D analogue once serum phosphate in target range

SERUM CALCIUM IN TARGET RANGE

1. Start or increase calcium-based binders
   - If calcium load is a concern: consider calcium acetate instead of calcium carbonate

2. <u>iPTH less than selected target</u>
   - Reduce or stop vitamin D analogue

   <u>iPTH in selected target range</u>
   - Maintain vitamin D analogue

   <u>iPTH greater than selected target</u>
   - Start or increase vitamin D analogue once serum phosphate in target range

SERUM CALCIUM GREATER THAN TARGET

1. Reduce calcium load: switch to calcium acetate or reduce calcium carbonate dose

2. Consider decreasing dialysate calcium

3. <u>iPTH less than selected target</u>
   - Stop or reduce vitamin D analogue

   <u>iPTH in selected target range</u>
   - Stop or reduce vitamin D analogue

   <u>iPTH greater than selected target</u>
   - Reduce Vitamin D analogue

4. Start or increase non-calcium binder

Approved for use by BCPRA Medical Advisory Committee August 2010

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SERUM PHOSPHATE IN SELECTED TARGET RANGE (follow trends)
If serum phosphate is less than 0.78 mmol/L, reduce phosphate binders and/or if nutritionally compromised, liberalize dietary phosphorus allowance.

SERUM CALCIUM LESS THAN TARGET

TREAT SYMPTOMATIC HYPOCALCEMIA:*
Consider oral calcium, dialysate calcium, vitamin D analogue

If not symptomatic

1. Stop non-calcium based binders and start or increase calcium-based binders.

2. <u>iPTH less than selected target</u>
   - Maintain or reduce vitamin D analogue

   <u>iPTH in selected target range</u>
   - Maintain vitamin D analogue

   <u>iPTH greater than selected target</u>
   - Start or increase vitamin D analogue

SERUM CALCIUM IN TARGET RANGE

1. Start or increase calcium based binder if serum phosphate in *high-normal* range
   - If calcium load is a concern: consider calcium acetate instead of calcium carbonate

2. <u>iPTH less than selected target</u>
   - Reduce or stop vitamin D analogue

   <u>iPTH in selected target range</u>
   - Maintain vitamin D analogue

   <u>iPTH greater than selected target</u>
   - Start or increase vitamin D analogue if calcium and phosphorus remain in low target range.

SERUM CALCIUM GREATER THAN TARGET

1. Reduce calcium load: switch to calcium acetate or reduce calcium carbonate dose

2. Consider decreasing dialysate calcium

3. <u>iPTH less than selected target</u>
   - Reduce or stop vitamin D analogue

   <u>iPTH in selected target range</u>
   - Reduce or stop vitamin D analogue

   <u>iPTH greater than selected target</u>
   - Reduce Vitamin D analogue

4. Start or increase non-calcium binder

COMMENTS

- Changes to phosphate binders and vitamin D analogue can be consecutive or concurrent depending on clinical situation.
- Initial dose reduction for calcium based phosphorus binders and /or vitamin D analogue is suggested to be about 50% but depends on the clinical situation.
- Repeat blood work is at the physician's discretion.
- Prescription of non-calcium based phosphorus binders should be reviewed and other treatment considered when hypercalcemia is corrected.
- **This tool does not consider treatment for post-parathyroidectomy (bone hunger) or uremic arteriolopathy (calciphylaxis).**

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Additional information about this discussion document:

* • Correction of hypocalcemia takes precedence over management of low iPTH levels and or high serum phosphorus. Treatment with calcium and vitamin D are indicated in this situation. Serum calcium slightly below normal may be well tolerated and not be of clinical significance.
- Serum calcium levels are used in this discussion rather than corrected calcium because corrected calcium levels are affected by albumin analysis and are not always reflective of ionized calcium levels. Use of corrected calcium over-identifies patients as hypercalcemic. Determination of ionized calcium levels may be indicated to verify hypercalcemia [4,5].
- Many factors affect the development of renal bone disease and vascular calcification. Observational studies report that total calcium load may play a role in disease progression. A maximum calcium load limit has not been established. Calcium acetate is recommended as the first line phosphorus binder due to its relatively low calcium content and superior phosphorus binding capacity, compared to calcium carbonate [8]. (Calcium carbonate: 200mg elemental Ca/ 500 mg tablet. Calcium Acetate:169 mg elemental Ca/667 mg tablet.)
- If lanthanum or sevelamer are prescribed in the absence of hypercalcemia their cost will not covered by BCPRA. The first month of lanthanum treatment may be covered by the lanthanum "smartpayment" program through Shire. If patients have third party health insurance the Genzyme Renassist program may cover a portion of sevelamer cost. For registered First Nations and recognized Inuit throughout Canada, sevelamer is a benefit (requires prior approval). www.healthcanada.gc.ca/nihb
- Mortality risk begins to increase when serum phosphate is above 1.67 mmol/L.7
- Clinicians may also consider Ca X P when planning treatment. KDOQI target for Ca X P is below 4.4 mmol/L [2]. KDIGO does not support the use of Ca X P in clinical practice [3].
- Serum phosphate levels may be allowed to increase to encourage improved nutritional intake and quality of life.
- Elevated serum phosphate, despite prescription of large doses of phosphorus binders, may be a result of poor adherence to the binder prescription. Reducing the dose of phosphorus binders may improve adherence and ultimately improve serum phosphate levels.
- Interpretation of iPTH levels is challenging since available assays do not specifically measure active PTH molecules and iPTH levels vary significantly over the day. It is important to follow iPTH trends and review symptoms when assessing the need for treatment. It may be prudent to initiate treatment when an increasing trend is noted even before iPTH has moved outside the target range. Elevated alkaline phosphatase levels, or an upward alkaline phosphatase trend may support diagnosis of active bone disease.
- Follow-up blood work is at the discretion of the physician and will depend on the severity of Ca/iPTH abnormality.
- Parathyroidectomy or calcimemetic therapy (cinacalcet) may be required to treat symptomatic hyperparathyroidism. Please refer to the BCPRA funding criteria for cinacalcet.
- Scientific information on the role of Vitamin D status/Vitamin D3 supplementation in bone mineral metabolism in CKD continues to emerge and is beyond the scope of this discussion.

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Prepared by: BCPRA Renal Dietitians Practice Group - December 2009

References:

1. Culleton B. F. et al. CSN Hemodialysis Clinical Practice Guidelines. *J Am Soc Nephrol*. 17: S1- S27, 2006

2. K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. *Am J Kidney Dis* 2003; 42 (Suppl 3): S1

3. KDIGO Clinical Practice Guidelines for Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease - Mineral Bone Disease (CKD-MBD). *Kidney International* (2009) 76 Suppl 113 www.kidney-international.org

4. Goransson L et.al. Albumin- corrected or ionized calcium in renal failure? What to measure? *Nephrol Dial Transplant* (2005) 20: 2126-2129

5. Clase C. et al. Albumin- corrected calcium and ionized calcium in stable hemodialysis patients. *Nephrol Dial Transplant* (2000) 15: 1841-1846

6. Yokum D et al. Evaluation of a phosphate management Protocol to Achieve Optimum Serum Phosphate Levels in Hemodialysis Patients. *J of Renal Nutr* Vol 18, No 6 2008 521-529

7. Block GA, Hulbert-Shearon TE, Levin NW, Port FK. Association of serum phosphorus and calcium x phosphate product with mortality risk in chronic hemodialysis patients: a national study. *Am J Kidney Dis*. 1998 Apr; 31(4):607-17

8. Levin A. et al. CSN Guidelines for the management of chronic kidney disease. *CMAJ*. November 18, 2008