GUIDELINES FOR THE TREATMENT OF HYPERPHOSPHATAEMIA & SECONDARY HYPERPARATHYROIDISM IN END STAGE RENAL FAILURE

Transplantation, Urology & Nephrology Directorate

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SECTION 1

INTRODUCTION

Rationale: Chronic kidney disease is an international public health problem affecting 5-10% of the world population. As kidney function declines, there is a progressive deterioration in mineral homeostasis, with a disruption of normal serum and tissue concentrations of phosphorus and calcium and changes in circulating levels of hormones. These include parathyroid hormone, 25-hydroxyvitamin D (25(OH) D), 1,25-dihydroxyvitamin D (1,25(OH)2D), and other vitamin D metabolites, fibroblast growth factor - 23 (FGF-23). As kidney function declines the ability of the kidneys to appropriately excrete a phosphate load is diminished, leading to hyperphosphataemia, elevated PTH, and decreased 1,25(OH)2D with associated elevations in the levels of FGF-23. The conversion of 25(OH)D to 1,25(OH)2D is impaired, reducing intestinal calcium absorption and increasing PTH. The kidney fails to respond adequately to PTH, which normally promotes phosphaturia and calcium reabsorption or to FGF-23 which also enhances phosphate excretion. Therapy is focused on correcting biochemical and hormonal abnormalities in an effort to limit their consequences.

Secondary hyperparathyroidism affects a significant number of haemodialysis patients, and metabolic disturbances associated with it may contribute to their higher mortality rate. This guideline has been formulated to provide a framework for medical, nursing staff and dieticians with regards to the treatment of hyperphosphataemia and secondary hyperparathyroidism in end stage renal disease.

Scope: This guideline is specifically for end stage renal failure, CKD stage 5 on renal replacement therapy. It is a guide for the multidisciplinary team, doctors, nurses, dieticians. It requires a multidisciplinary approach. The nursing team in conjunction with the medical team will review blood levels and adjust/change drug levels as necessary. Dietitian in conjunction with the nursing team will review and educate patients with regards to their diet.

Principles (Beliefs): The ultimate goal of treating SHPT is to normalise mineral metabolism, prevent bone disease and prevent extraskeletal manifestations of the altered biochemical process. It is important to identify SHPT early. Earlier identification and assessment of SHPT will improve bone and mineral metabolism in chronic kidney disease and reduce its associated complications such as fractures, pain and cardiovascular calcification.
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SECTION 2

The statement of the standard that is to be achieved is as follows.

> IDENTIFY TARGET BLOOD RANGES FOR CKDMBD, STAGE 5 ON RENAL REPLACEMENT THERAPY.

> DISCUSS THE CONTROL OF SERUM PHOSPHATE.

> CALCIUM BASED PHOSPHATE BINDERS
  > NON CALCIUM BASED PHOSPHATE BINDERS

> DISCUSS THE CONTROL OF SECONDARY HYPERPARATHYROIDISM

> ACTIVE VITAMIN D ANALOUGES

> CALCIMIMETIC
If commencing or adjusting drug therapies consider previous trends and not single readings in isolation.

Target Blood Ranges

<table>
<thead>
<tr>
<th>Stage 5 CKD</th>
<th>Phosphate (mmol/L)</th>
<th>Corrected Calcium (mmol/L)</th>
<th>PTH Pg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.8-1.5</td>
<td>2.2-2.6</td>
<td>150-500</td>
<td></td>
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</table>

Control of Serum Phosphate

(1) Refer early for dietary advice. Dietary phosphate restriction is essential for phosphate control.

(2) Commence phosphate binders when dietary restrictions are unable to maintain serum phosphate < 1.6mmol/L.

Calcium Based Phosphate Binders

- Calcium containing phosphate binders are the initial binders of choice if calcium < 2.6
- Titrate up dose of calcium containing binders as required to achieve adequate phosphate control <1.5mmol/L

<table>
<thead>
<tr>
<th>Binder</th>
<th>Form / Elemental Ca$^{2+}$</th>
<th>Max Daily Dose</th>
<th>Starting Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Acetate (Phosex)</td>
<td>500mg tablet / 125 mg 1g tablet / 250mg</td>
<td>TTT QDS</td>
<td>TT TDS T TDS</td>
</tr>
<tr>
<td>Calcium Acetate &amp; Magnesium Carbonate (Osvaren)</td>
<td>435mg 235mg tab / 110 mg Ca, 60mg Mg</td>
<td>TTT QDS</td>
<td>T TDS Monitor serum Mg</td>
</tr>
<tr>
<td>Calcium carbonate (Calcichew)</td>
<td>Not routinely used</td>
<td></td>
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</tbody>
</table>

- Keep daily elemental calcium intake from binders to less than 1500 mg.
- Total elemental calcium from diet and binders not to exceed 2000mg/day.
GUIDELINES FOR THE TREATMENT OF HYPERPHOSPHATAEMIA & SECONDARY HYPERPARATHYROIDISM IN END STAGE RENAL FAILURE

❖ Non Calcium Based Phosphate Binders

Consider non-calcium containing binder therapy in following circumstances:

- Baseline serum calcium > 2.6mmol/L.
- Baseline low PTH < 150pg/ml.
- Evidence of tissue/vascular calcification.
- As add on to calcium containing binder therapy if target phosphate not achieved despite maximum dose usage.

Choice of binder depends or preparation the patient prefers to take.

Consider switching to alternate phosphate binder if poor compliance suspected or gastrointestinal side effects reported.

<table>
<thead>
<tr>
<th>Binder</th>
<th>Form</th>
<th>Max Daily Dose</th>
<th>Starting Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lanthanum Carbonate (Foznol – crush/chew)</td>
<td>250mg, 500mg, 750mg, 1g tablet</td>
<td>3750mg</td>
<td>500mg TDS After meals</td>
</tr>
<tr>
<td>Sevelamer Carbonate (Renvela – swallow whole)</td>
<td>800mg tablet 2400mg sachet</td>
<td>TTT TDS 3 sachets</td>
<td>TTT TDS T TDS</td>
</tr>
<tr>
<td>Sevelamer Hydrochloride (Renagel – swallow whole)</td>
<td>800mg tablet</td>
<td>TTT TDS</td>
<td>TTT TDS With meals</td>
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</tbody>
</table>

If dietary measures/binders fail to control phosphate effectively consider increasing frequency & duration of dialysis.
GUIDELINES FOR THE TREATMENT OF HYPERPHOSPHATAEMIA & SECONDARY HYPERPARATHYROIDISM IN END STAGE RENAL FAILURE

● **Control of Secondary Hyperparathyroidism**

Serial follow up of PTH levels should be performed at three month intervals to assess the continued control of disease

(1) Ensure optimal control of serum phosphate through dietary restrictions and phosphate binders.

(2) If PTH remains > 500pg/ml or fails to trend downwards despite achieving adequate phosphate control ie. <1.5mmol/L commence/increase active vitamin D analogues.

**Vitamin D analogues should not be commenced until satisfactory phosphate control is achieved**

● **Active Vitamin D Analogues**

• Alphacalcidol (*One Alpha*) is the vitamin D analogue of choice in the treatment of secondary hyperparathyroidism.

• Initial dose of 0.25mcg, titrated up to 1mcg, if calcium remains within range.

• If PTH remains > 500pg/ml or fails to trend downwards despite use of alphacalcidol consider swapping to Paricalcitol, (on 2 consecutive readings).

• Consider using paricalcitol in preference to alphacalcidol if serum calcium levels are running at higher end of normal reference range

• Paricalcitol (*Zemplar*) should be administered orally.
Zemplar | Dose | Max Daily Dose | Starting Dose
---|---|---|---
Oral | 1 mcg tablet 2 mcg tablet | 4mcgs od | 2 mcq od

- Titrate dose of Paricalcitol upwards until PTH ≤ 500pg/ml
- Pre-dialysis calcium, phosphate should be monitored weekly once patients are commenced on paricalcitol.
- Monthly PTH serum readings should be taken once patients are commenced on paricalcitol.
- If PTH < 150pg/ml consider the following options, reduce or stop vitamin D therapy, switch to non-calcium containing binders, lower dialysate calcium concentration in order to avoid adynamic bone disease.
- If PTH remains above target and further dose escalation in vitamin D analogue limited by serum calcium > 2.6 consider the following options:
  - PTH > 500pg/ml or fails to trend downwards on 2 consecutive readings: consider adding cinacalcet to conventional therapy (binders/vitamin D).
  - Consider parathyroidectomy if refractory SHPT (PTH 1000pg/ml) despite cinacalcet use.
Cinacalcet (Mimpara)

- Cinacalcet is indicated for treatment of SHPT.
- It is associated with less hypercalcaemia compared to vitamin D3 analogues.
- Cinacalcet should be considered in patients with PTH > 500pg/ml and in whom further dose escalation of vitamin D analogue is limited by elevated calcium (>2.6 mmol/L).

<table>
<thead>
<tr>
<th>Mimpara</th>
<th>Dose</th>
<th>Max Daily Dose</th>
<th>Starting Dose</th>
</tr>
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<tbody>
<tr>
<td>Oral</td>
<td>30mg</td>
<td>6 Tabs</td>
<td>30mg (od)</td>
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<td>60mg</td>
<td>3 Tabs</td>
<td>Taken &gt;12 hrs before blood draw</td>
</tr>
<tr>
<td></td>
<td>90mg</td>
<td>2 Tabs</td>
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</table>

- Starting dose 30mg od titrating upwards every 4 weeks until PTH ≤ 500pg/ml or pt on max dose 180mg od. Titrate downwards once satisfactory control is achieved.
- Pre-dialysis calcium/phosphate/magnesium should be monitored weekly once patients are commenced on cinacalcet.
- Monthly PTH serum readings should be taken once patients are commenced on cinacalcet.
- If on Zemplar and/or Mimpara and PTH low (<150):
  - Reduce/stop cinacalcet.
  - Switch to non-calcium containing binders.
  - Consider reduce/stop vitamin D analogue.
  - Use low calcium dialysate bath eg. 1mmol/L.

If commencing or adjusting drug therapies consider result trends of a least two consecutive month readings.

If changes are made in OPD appointments please inform nursing staff in the relevant HD or PD Unit.
**SECTION 4**

**Treatment of Hyperphosphataemia**

- **Serum Phosphate > 1.5 mmol/L**
  - Refer to dietitian
  - Dietary phosphate restriction is crucial in managing elevated serum phosphate

- **Serum Phosphate 0.8 – 1.5mmol/L**
  - Monitor monthly

- **Serum phosphate >1.5 mmol/L**
  - Normal serum Calcium 2.2 – 2.6mmol/L
  - Elevated serum Calcium > 2.6mmol/L
    - Low baseline PTH < 150pg/ml
    - Evidence of tissue/vascular calcification

**Calcium Based Binders**

- **Calcium Acetate**
  - Start dose 1g TDS

- **Osraven**
  - Start dose T TDS

**Non Calcium Based Binders**

- Select binder depending on form pt prefers

- **Lanthanum Carbonate (Foznol)** - Chew or crush
  - Start dose – 500mg tablet - T TDS after meals

- **Sevelamer Carbonate (Renvela)** - swallow whole
  - Start – TTT TDS (800mg tablet) or Sachet T TDS before meals

- **Sevelamer Hydrochloride (Renagel)** - swallow whole
  - Start dose - 2400 mg - TDS before meals

If dietary measures & binders fail to control phosphate effectively consider increasing dialysis frequency or duration.
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TREATMENT OF ELEVATED PTH

**Serum PTH > 500 pg/ml**
Despite Alfacalcidol 0.25 mcg/Day

Ensure optimal control of serum phosphate through dietary restriction and binders. (Refer to Treatment of hyperphosphataemia Guidelines)

- **Serum PTH 150 - 500 pg/ml**
  - Monitor at 3/12 intervals
  - Titrate oral Alfacalcidol to max dose 1 mcg OD
  - Monitor at 1/12 intervals
  - **Vit D analogues should be held if Corrected Ca\(^{2+}\) +/- or serum phos remain elevated**

- **Corrected Ca\(^{2+}\) <2.6 mmol/L**
  - PTH > 500pg/ml or not trending downwards on 2 consecutive months
  - Monitor at 3/12 intervals

- **Corrected Ca\(^{2+}\) >2.6 mmol/L**
  - PTH > 500pg/ml or not trending downwards on 2 consecutive months
  - *Paricalcitol*
    - Oral 2 mcg OD
    - (Titrate to 4 mcg OD)
  - Monitor at 3/12 intervals

- **PTH > 500pg/ml or not trending downwards on 2 consecutive months**
  - Add *Cinacalcet*
    - Start at 30mg OD & titrate up.
    - Consider switching Paricalcitol to 1Alpha (0.25-1mcg/D)
    - Monitor at 1/12 intervals

- **PTH 150 – 500 pg/ml**
  - PTH not trending towards or remains > 500 pg/ml +/- Ca\(^{2+}\) > 2.6 on 2 consecutive readings
  - Monitor at 3/12 intervals

- **Serum PTH < 150 pg/ml**
  - Reduce/stop Cinacalcet
  - Switch to non calcium based binders
  - Consider reduce/stop vit D analogue
  - **Corrected Ca\(^{2+}\) <2.6 mmol/L**

Consider parathyroidectomy if refractory SHPT (PTH > 1000pg/ml)
SECTION 5

DISTRIBUTION
A copy of the guideline will be circulated to the relevant areas by the Divisional Nurse Manager and Consultants. The Clinical Nurse Manager in each area is responsible to ensure all staff access and read the guideline. The guideline will also be available on the renal intranet webpage. The Consultant staff are responsible to ensure that medical staff access and read the guideline.

SECTION 6

FILING
A copy will be filed in the guideline and procedure book folder in each unit. The master copy will be filed in the Divisional Nurse Managers office.

SECTION 7

REVIEW
This guideline will be reviewed in two years, February 2013.

SECTION 8

SUPERSEDED/OBSOLETE DOCUMENTS
This is an updated version of Guidelines for Treatment of Hyperphosphataemia & SHPT and replaces all previous versions.
**DEVELOPMENT AND CONSULTATION PROCESS**

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<td>Informal meetings &amp; emails between Caroline Brummel, Brian Carey &amp; Oonagh Deeney following identification of required policy review.</td>
<td>March - November 2011</td>
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<td>Subsequent development of treatment flow diagrams</td>
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<td>Informal meeting between Prof Conlon, Caroline Brummel, Brian Carey &amp; Oonagh Deeney to discuss proposed policy &amp; treatment flow diagrams.</td>
<td>December 2011</td>
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<td>February 2012</td>
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<td>March 2012</td>
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<td>April 2012</td>
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SECTION 10

REFERENCE DOCUMENTS


