

1. Introduction

Secondary hyperparathyroidism is an important complication of chronic kidney disease. Despite improvements in medical management with phosphate control, vitamin D analogues and, in selected cases, calcimimetics (i.e. cinacalcet), many patients eventually require surgical parathyroidectomy.

Post operatively, there is a risk of hypocalcaemia as the bone healing and remineralisation leads to incorporation of large amounts of calcium into the skeleton. In the worst case scenario, this can lead to symptomatic hypocalcaemia including seizures. For some time in the Leicester Renal/Transplant service there has been a guideline for the immediate postoperative management of hypocalcaemia often involving administration of large amounts of intravenous calcium via a central line but no written guidance on the management post hospital discharge.

An audit of post-operative control of serum calcium has shown huge variation in the dose of alfacalcidol prescribed and fluctuating serum calcium concentrations with both hypo- and hypercalcaemia persisting over many months.

The purpose of this guideline is to try to standardise the peri-operative care of patients with CKD undergoing surgical parathyroidectomy to prevent these problems.

2. Scope

All patients with chronic kidney disease (peritoneal dialysis, haemodialysis or chronic kidney disease stage 4/5) who are undergoing surgical parathyroidectomy for uncontrolled secondary hyperparathyroidism (see guideline 'Management of renal osteodystrophy for indications for surgical intervention').

3. Recommendations, Standards and Procedural Statements

3.1 Pre –operativemanagement

- Patients identified for parathyroidectomy should be prescribed oral alfacalcidol 5 micrograms once daily for 3 days prior to procedure (last dose on the day before of surgery) to induce gastrointestinal calcium receptors. This prescription should be issued at the pre-assessment visit. However, if adjusted calcium $>2.8\text{mmol/L}$ at pre-assessment then this loading should be withheld.
- Pre-operative calcium and phosphate should be checked. The pre-assessment nurse/doctor should telephone the patient to tell them not to take the medication if the screening adjusted calcium is $>2.8\text{mmol/L}$.
- Continue on the usual phosphate binder at this stage
- If the patient is on cinacalcet, this should be stopped 3 days before admission.
- Arrange for ENT team to check vocal cords pre-anaesthetic if requested in clinic letter.
- Inform histopathology department the day before surgery that urgent frozen section will be sent from theatre if requested in clinic letter.

- Methylthioninium Chloride (previously known as Methylene blue) infusion: 3mg/kg given as an intravenous infusion in 500mls of 5% glucose (**must not be with normal saline**) which should be administered over 60 minutes and must be started one hour before surgery (same dose for primary/tertiary hyperparathyroidism)
 - for example, for a patient of 70 kg of body weight, the amount of Methylthioninium chloride will be $3 \times 70 = 210$ mg to be mixed with 500mls of 5% dextrose & needs to be infused over an hour

Warnings and precautions:

Methylthioninium chloride is best avoided in patients who are taking, or have recently been treated with SSRI antidepressants (such as citalopram, fluoxetine, paroxetine and sertraline), clomipramine, mirtazepine, buspirone, bupropion or venlafaxine as this may enhance CNS toxicity. This should be used with extreme caution in patients with brittle diabetes.

If there is a compelling reason to use methylthioninium chloride, patients should be monitored for CNS effects for up to 4 hours post administration.

Rarely, anaphylaxis may occur whilst using this dye. Therefore, this product should only be used in clinical areas where there is access to adrenaline injection (1:1000), hydrocortisone (sodium succinate) injection and chlorpheniramine injection to treat anaphylaxis as per Grey Book guidance

Side- effects:

Hypotension, hypertension, cardiac arrhythmias, tachycardia, chest pain and shortness of breath, nausea, vomiting, abdominal pain, headache, dizziness, tremors, confusion, sweating, blue colouration of urine, faeces and saliva.

Monitoring:

The patient should have their blood pressure and pulse checked at the beginning and at the end of the infusion. Closer monitoring of capillary blood glucose levels is warranted in diabetic patients.

Patients should be advised that their urine, faeces and saliva may appear blue after the infusion, but this will subside with time.

3.2 Immediate post –operative care

- Serum calcium and phosphate should be checked 6 hourly for the first 48 hours and then 12 hourly until stable.
- The frequency of monitoring should be decided based on the serum calcium concentration and its rate of change. Adjust timing of blood sampling such that haemodialysis patients have their bloods taken pre dialysis.
- IV calcium gluconate infusion may need to be administered during the immediate post - operative period (see appendix 1).
 - Change to oral calcium when patient is able to take and retain medications orally. KDOQI guidelines recommend 1-2g of elemental calcium 3 times a day which is approximately equal to 25-50mmol of calcium three times per day. Preferably Calvive 1000 (25 mmol calcium per tablet) 2 tablets tds not to be given with meals.
- The choice of the calcium supplement should be tailored to the patient (see table for calcium content of different preparations). The patient's acceptability of the formulation is important for adherence and this has to be determined before discharge.
- Oral calcium supplements should be prescribed to be taken between meals to maximise absorption

Calcium Supplements (1 mmol is equal to 40mg of elemental calcium)

Oral	Calcium Content
Adcal (chewable)	15 mmol / tablet
Calcichew (chewable)	12.6 mmol / tablet
Calvive (soluble)	25 mmol / tablet
Calcichew forte(chewable)	25 mmol / tablet
Phosex (swallow whole)	6.2 mmol/tablet

- Continue alfacalcidol 5 micrograms twice daily (BD) orally unless calcium levels are above 2.5 mmol/L in which case the dose should be reduced
- Phosphate binders – patients on sevelamer or lanthanum should be switched to calcium containing phosphate binders unless they have previously been demonstrated to be intolerant of these or they have evidence of vascular calcification or calciphylaxis.
- Patients on calcium containing phosphate binders should continue their usual treatment with meals unless they develop hypophosphataemia.
- Increase calcium supplement by 50% if calcium continues to fall and half if calcium starts to rise.
- Check the serum magnesium and PTH along with calcium day 1 morning post op blood test and if Mg³⁺ low, discuss with SpR/Consultant for supplementation
- If hypocalcaemia is resistant to treatment, then check serum magnesium concentration and if necessary replace intravenously.

3.3 Management of serum calcium and alfacalcidol/calcium supplementation after discharge

Discharge dose of calcium supplement and alfacalcidol varies among patients. The dose will be dependent on the patient's serum calcium and the trend in rise or fall of serum calcium prior to discharge.

- On discharge serum calcium levels should be taken two to three times a week until stable (usually on haemodialysis)
- The responsible consultant nephrologist for the patient must be informed of the discharge and with the ward team a plan for monitoring the serum calcium should be agreed
- Oral calcium supplements and alfacalcidol dose should be continued and adjusted according to the serum calcium results after each calcium check
- Discharge dose of calcium supplement and alfacalcidol varies among patients. The dose will be dependent on the patient's serum calcium and the trend in rise or fall of serum calcium prior to discharge.

Frequency of serum calcium monitoring post-parathyroidectomy following hospital discharge

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Weeks	Frequency	Comments
1-2	X2-3	With dialysis if HD patient
3-4	X2	
4-6	X1	

3.3.1 Hospital/Satellite dialysis patients: The nurse in charge(or deputy) and the relevant consultant of the patient in the unit needs to be contacted and informed to check serum calcium before each dialysis (3 times weekly) for at least first 2 weeks post discharge then reducing frequency as above unless calcium very unstable. The serum calcium and phosphate concentrations measured during this period need to be discussed with a registrar or consultant even if within normal range of serum calcium to identify trends in increase or decrease of levels earlier on to make dose adjustments to medication. The dosage of alfacalcidol, calcium supplements and phosphate binders should be recorded in the template form (see appendix) and the PROTON medication screen MUST be updated.

3.3.2 Home haemodialysis/peritoneal dialysis: Discharge arrangement to monitor serum calcium levels 2 times weekly for the first 2 weeks needs to be discussed and arranged with the patient's community nurse. The relevant renal community nurse and nephrology consultant needs to be informed to permit checking of results and dose adjustments. The dosage of alfacalcidol, calcium supplements and phosphate binders should be recorded in the template form (see appendix) and PROTON medication screen updated.

3.3.3 Non dialysis patients: Discharge arrangement to monitor serum calcium levels 2 times weekly for the first 2 weeks needs to be discussed and arranged with the patient's GP or the patient provided with forms to have blood tests. The relevant renal community nurse and nephrology consultant needs to be informed to permit checking of results and dose adjustments. The dosage of alfacalcidol, calcium supplements and phosphate binders should be recorded in the template form (see appendix) and PROTON medication screen updated.

3.4 Guidance for post discharge dose changes

The dosing of alfacalcidol and calcium supplements post operatively is difficult even for experienced clinicians. Audits have shown that both hypo- and hyper-calcaemia are common. Trends in concentration are more important than absolute values. Patients who become hypercalcaemic in large doses of alfacalcidol/calcium supplements will frequently become hypocalcaemia if these are withdrawn completely rather than dose reduced. The following advice is for guidance:-

3.4.1 If hypocalcaemia(<2.20mmol/L) or reducing trend in calcium concentration

- Check adherence and increase calcium supplement by 50%.
- Alfacalcidol dose to increase up to a maximum of 5 micrograms bd but note it takes 3 days to observe effect of increase in dose. Alfacalcidol product specification recommend increasing dose in increments of 0.25 – 0.5 micrograms but if taking 2micrograms or more change dose by 1microgram.
- If patient is symptomatic and calcium concentrations are very low (usually below 1.90mmol/L), this may require hospital admission for intravenous calcium gluconate infusion.
- Check magnesium levels and replace intravenously if recurrent /resistant hypocalcaemia.

3.4.2 If hypercalcaemia(>2.60mmol/L) or increasing trend in calcium levels

- Reduce dose of calcium supplement and alfacalcidol dose by 50%.

- Stop calcium supplement and alfacalcidol if serum calcium is equal to or more than 3.0 mmol/L but these should be restarted at half previous dose once calcium falls to <2.6mmol/L
- It usually takes 3 days to observe effect of decrease or stop in dose of alfacalcidol.
- When medications are stopped re-prescribe alfacalcidol at half the initial dose when serum calcium levels reach 2.5mmol/L. Calcium supplements can be added if required depending on the trend in calcium levels.

4. Education and Training

Medical staff from nephrology and transplant service and nursing staff (ward nurses, haemodialysis nurses and renal community team) should be familiar with guideline and access it for specific advice on dosing.

5. Monitoring and Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead
Control of calcium post parathyroidectomy	Audit	Biannually	Transplant medical staff

6. Legal Liability Guideline Statement

Guidelines issued and approved by the Trust are considered to represent best practice. Staff may only exceptionally depart from any relevant Trust guidelines and always only providing that such departure is confined to the specific needs of individual circumstances. In healthcare delivery such departure shall only be undertaken where, in the judgement of the responsible healthcare professional it is fully appropriate and justifiable - such decision to be fully recorded in the patient's notes

7. Supporting Documents and Key References

None applicable

8. Key Words

Parathyroidectomy, renal failure, alfacalcidol, calcium

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Date	Issue Number	Reviewed By	Description Of Changes (If Any)
13Oct 2015	2	G Warwick/Atul Bagul/Maria Martinez	Reviewed; use of methylthioninium chloride added; starting dose of alfacalcidol post-op increased; minor other changes
27Jan19	3	Richard Baines	Minor changes only.
26 May 2022	4	Amy Page/Maria Martinez/ Atul Bagul	Strength and volume of methylthioninium chloride removed; amended Sandocal to Calvive
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APPENDIX 1 - PROTOCOL FOR INTRAVENOUS CALCIUM POST PARATHYROIDECTOMY

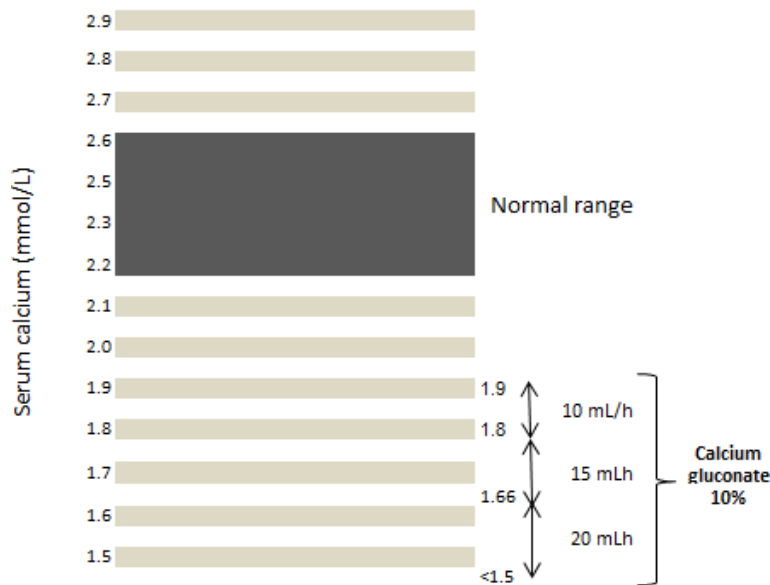
Criteria for use of intravenous calcium:

- Severe symptoms (paraesthesia / muscle cramps / carpo-pedal spasm / laryngeal stridor / convulsions / prolonged QT interval / arrhythmias / hypotension)
- It may be considered if the corrected calcium is less than 1.9mmol/L or
- If the corrected calcium is falling rapidly i.e. >10% over 6 hrs and the development of significant hypocalcaemia can be predicted by the preceding trend.
- **Care must be taken to ensure intravenous calcium is not extravasated; if venous access is not secure then a central line may be required and this should be discussed with the Renal/Transplant Consultant**
- Emergency situations - Give 10mL of 10% calcium gluconate (2.2mmolcalcium) no faster than 2mL/min(i.e. over at least 5mins, ECG monitoring recommended); this can be given peripherally.

Intravenous calcium infusion - Instructions for use:

- Check calcium immediately post-operatively and then 4-6hrly for 48-72hrs till stable
- This MUST ALWAYS be infused via a central line
- Set up calcium infusion: 50 mL calcium gluconate 10%
- Adjust infusion rate according to serum calcium and table; plot values on graph

Calcium gluconate infusion following parathyroidectomy



Serum calcium mmol/L	Infusion rate ml/hr
<1.65	20
1.66-1.80	15
1.90-1.80	10
>1.90	0

