Kent and Medway Cancer Collaborative

Network Guidance Document

Hypercalcaemia Guidelines

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Contents

1.0 Signs and symptoms of hypercalcaemia of malignancy

Hypercalcaemia is defined as a serum calcium concentration of 2.65mmol/L(or higher) on two occasions, following adjustment for the serum albumin concentration. It might be classified according to severity:

- Mild-adjusted serum calcium concentration of 2.65-3.00 mmols/L
- Moderate- adjusted serum calcium concentration of 3.01-3.40mmols/L
- Severe-adjusted serum calcium concentration of greater than 3.40mmol/L

In malignancy, hypercalcaemia most commonly results from direct bony invasion by tumour cells rather than humorally mediated hypercalcaemia.

1.1 Symptoms

◦Skeletal — bone pain, fractures (osteoporotic in hyperparathyroidism or pathological in malignancy).
◦Neuromuscular and neuropsychiatric — drowsiness, delirium, coma, fatigue, muscle weakness, impaired concentration and memory, depression, and neurological signs (for example upper motor neurone deficits and ataxia).
◦Gastrointestinal — nausea, vomiting, anorexia, weight loss, constipation, abdominal pain, peptic ulcer, and pancreatitis.
◦Renal — polyuria, polydipsia, and dehydration; renal colic and renal impairment.
◦Cardiovascular — hypertension, and shortened QT interval on electrocardiogram (ECG).
◦Other — itching, keratitis, conjunctivitis, and corneal calcification.

1.2 Patients at risk

Tumour types associated with hypercalcaemia
Lung 35%
Breast 25%
Haematological 14%
Squamous (head & neck) 6%
Genito-urinary 6%
Other 15%

2.0 Management of malignant hypercalcaemia

1. Calcium adjusted for albumin
   serum Ca mmol/L + [(40-albumin) x 0.02]

2. Assess hydration state clinically and according to U&E.
   Commence IV fluids, 4-6 litres sodium chloride 0.9% per 24 hours if dehydrated.
   Monitor for fluid overload if renal impairment or elderly
   Re-assess corrected calcium level. If < 3.0 after hydration, it is likely that the patient will still require iv bisphosphonate. If patient is adequately hydrated and has a normal urea then initiate bisphosphonate as soon as possible.

3. Pamidronate:

Corrected Calcium	Pamidronate dose	Administration
Up to 3.0 mmol/l	15-30mg	250ml Sodium Chloride 0.9% over 30 minutes
3.0 – 3.5 mmol/l	30-60mg	250ml Sodium Chloride 0.9% over 1 hour
3.5 – 4.0 mmol/l	60-90mg	500ml Sodium Chloride 0.9% over 90 minutes
>4.0 mmol/l	90mg	500ml Sodium Chloride 0.9% over 90 minutes

A significant decrease in serum calcium is generally observed 24-48 hours after administration of Disodium Pamidronate Injection, and normalisation is usually achieved within 3-7 days. Dose can be repeated at 3 - 4 week intervals.

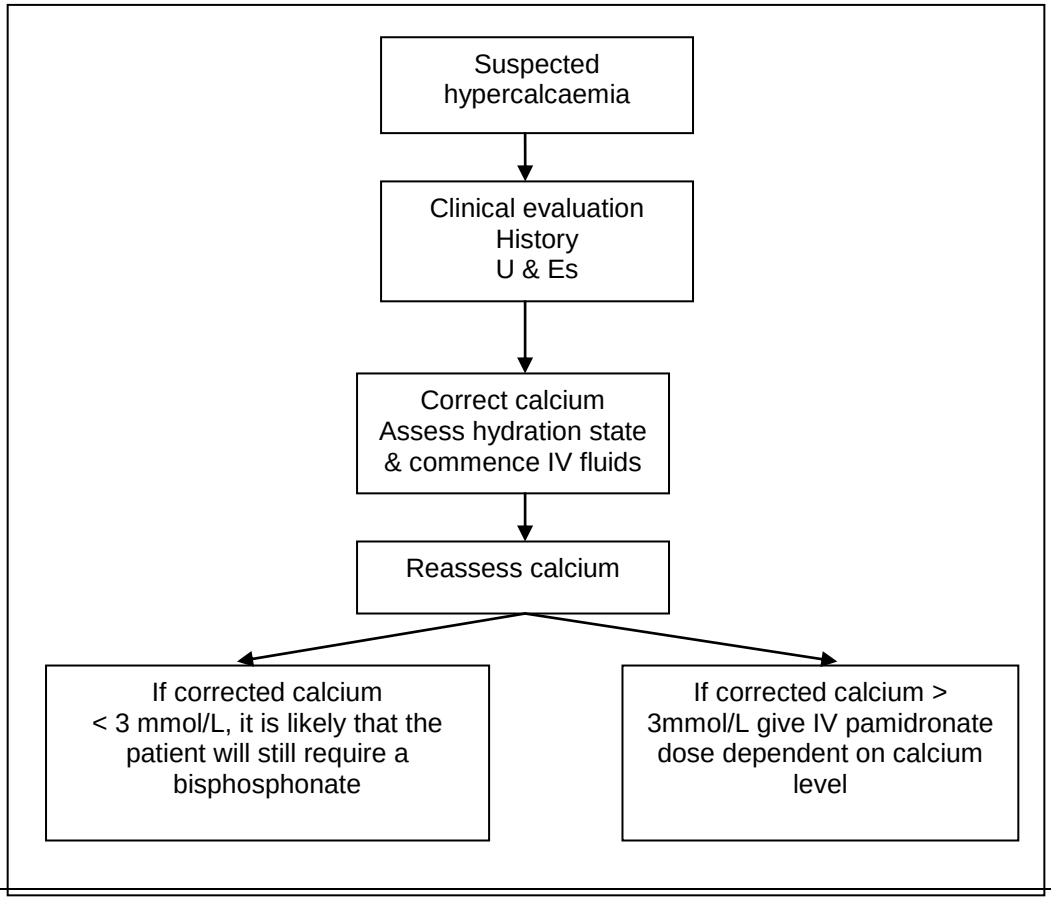
The total dose of pamidronate may be administered either as a single infusion or in multiple infusions over 2 – 4 consecutive days.
The maximum dose per treatment course is 90mg for both initial and repeated courses.

Dosage in renal failure (SPC): Pamidronate should not be administered to patients with severe renal impairment (creatinine clearance < 30 mL/min) unless in cases of life-threatening tumour-induced hypercalcaemia where the benefit outweighs the potential risk. It is recommended that for patients with established or suspected renal impairment, the infusion rate should not exceed 20mg/hour.

4. Zoledronic acid (Zometa®) can be used routinely for tumour-induced hypercalcaemia. The recommended dose in hypercalcaemia (albumin-corrected serum calcium ≥ 12.0 mg/dl or 3.0 mmol/l) is a single dose of 4 mg zoledronic acid.

5. Potential side effects of bisphosphonates –
For full list, see manufacturers' SPCs.
Very common (>10%): transient pyrexia and influenza-like symptoms (more common with IV nitrogen-containing bisphosphonates), fatigue, headache, anxiety, hypertension, anaemia, thrombocytopenia, cough, arthralgia, myalgia, bone pain, asymptomatic hypocalcaemia, hypomagnesaemia, hypophosphataemia. Oral preparations in particular may cause anorexia, dyspepsia, nausea, vomiting, abdominal pain, diarrhoea or constipation.
Common (<10%, >1%): sleep disturbance, psychosis, tachycardia, atrial fibrillation or flutter, syncope, dyspnoea, leucopenia, infusion site reactions, deterioration in renal function, increased serum creatinine, hypokalaemia.
Rare (<0.1%, >0.01%): ocular inflammation, angioedema, collapsing focal segmental glomerulosclerosis (**disodium pamidronate**), nephrotic syndrome (**disodium pamidronate**), symptomatic hypocalcaemia (e.g. tetany).
Very rare (<0.01%): anaphylaxis, bronchospasm, osteonecrosis of the jaw.

3.0 Diagnostic Algorithm for Hypercalcaemia of Malignancy



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Document Administration

Approval Record

Approval		
Date	**Name / Title**	**Signature**
4th May 2011	Circulated to Acute Oncology Group with 2 weeks to comment	
24th May 2011	Final document distributed to Acute Oncology Group	
May 2018	KMCC Chemotherapy Group - discussed at meeting, minor changes circulated via email	

Enquiries

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Document Location

The document is located in the Kent and Medway Cancer Collaborative office, in electronic format.
The document can also be found on the Kent and Medway Cancer Collaborative website.

Revision History

Date	Version	Status	Author	Summary of Changes
April 2011	1	Draft	Kate Miller	Comments incorporated from Acute Oncology Group
May 2011	1.1	Draft	Kate Miller	Comments incorporated from Acute Oncology Group
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ORIGINATORS OF THIS EVIDENCE ITEM

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Updated by E Parry 2018