Acute Hypercalcaemia

Introduction:
Under physiological conditions, serum calcium concentration is tightly regulated. Abnormalities of parathyroid function, bone resorption, renal calcium reabsorption or dihydroxylation of vitamin D may cause regulatory mechanisms to fail and serum calcium may rise. Serum calcium is bound to albumin, and measurements should be adjusted for serum albumin.

Severity of hypercalcaemia

<table>
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<tr>
<th>Range</th>
<th>Description</th>
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<td>&lt; 3.0 mmol/l</td>
<td>often asymptomatic and does not usually require urgent correction.</td>
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<td>3.0 to 3.5 mmol/l</td>
<td>may be well tolerated if it has risen slowly, but may be symptomatic and prompt treatment is usually indicated.</td>
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<td>&gt; 3.5 mmol/l</td>
<td>requires urgent correction due to the risk of dysrhythmia and coma.</td>
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Clinical features of hypercalcaemia:
- Polyuria and thirst
- Anorexia, nausea and constipation
- Mood disturbance, cognitive dysfunction, confusion and coma
- Renal impairment
- Shortened QT interval and dysrhythmias
- Nephrolithiasis, nephrocalcinosis
- Pancreatitis
- Peptic ulceration
- Hypertension, cardiomyopathy
- Muscle weakness
- Band keratopathy

Causes:
- Ninety percent of hypercalcaemia is due to primary hyperparathyroidism or malignancy.

Less Common causes include:
- Thiazide diuretics
- Rhabdomyolysis
- Tertiary hyperparathyroidism
- Thyrotoxicosis
- Hypervitaminosis D
- Lithium
- Immobilisation
- Non-malignant granulomatous disease
- Adrenal insufficiency
- Milk-alkali syndrome
- Hypervitaminosis A
- Theophylline toxicity
- Familial hypocalciuric hypercalcaemia
- Phaeochromocytoma
**Investigation:**

- **History**
  - Symptoms of hypercalcaemia and duration
  - Symptoms of underlying causes – e.g. weight loss, night sweats, cough
  - Family history
  - Drugs including supplements and over-the-counter preparations

- **Examination**
  - Assess for cognitive impairment
  - Fluid balance status
  - For underlying causes – including neck, respiratory, abdomen, breasts, lymph nodes

- **ECG**
  - Look for shortened QT interval or other conduction abnormalities

- **Bloods**
  - Calcium adjusted for albumin
  - Phosphate
  - PTH
  - Urea and electrolyte

| High calcium and high PTH = primary or tertiary hyperparathyroidism |
| High calcium and low PTH = malignancy or other rarer causes |

**Management:**

**Rehydration**

| Intravenous 0.9% saline 4-6 litres in 24h |
| o Monitor for fluid overload if renal impairment or elderly |
| o Loop diuretics rarely used and only if fluid overload develops; not effective for reducing serum calcium |
| o May need to consider dialysis if severe renal failure |

**After rehydration: intravenous bisphosphonates**

| Zoledronic acid 4mg over 15 minutes |
| OR Pamidronate 30 to 90mg (depending on severity of hypercalcaemia) at 20mg/hr |
| OR Ibandronic acid 2 to 4mg |

- Give more slowly and consider dose reduction in renal impairment
- Monitor serum calcium response – will reach nadir at 2 to 4 days
- Can cause hypocalcaemia if vitamin D deficiency or suppressed PTH
**Second line treatments**

- Glucocorticoids (inhibit 1,25OHD production)
  - In lymphoma, other granulomatous diseases or 25OHD poisoning
  - Prednisolone 40mg daily
  - Usually effective in 2 to 4 days
- Calcitonin
  - Can be considered if poor response to bisphosphonates
- Calcimimetics
  - Licensed for hypercalcaemia due to primary hyperparathyroidism, parathyroid carcinoma or renal failure

**References:**


This information is provided by the Society for Endocrinology’s Clinical Committee, February 2013, and will be reviewed annually.