Hypercalcaemia in Adult Patients in Secondary Care

Mild to moderate hypercalcaemia (<3.0mmol/L) may be asymptomatic. Symptoms of polyuria, thirst, anorexia, weakness, nausea and vomiting become more likely as serum calcium rises from 3.0 to 3.5 mmol/L. Hypercalcaemia should be part of the investigation of unexplained deterioration in renal function or dehydration. Very high serum calcium is most often due to neoplastic disease, but other causes are possible.

90% of hypercalcaemia is due to primary hyperparathyroidism or malignancy[1].

If patient has malignant hypercalcaemia, refer to Management of Malignant Hypercalcaemia guideline.

Severity of hypercalcaemia[1]:

<3.0mmol/L	Often asymptomatic and does not usually require urgent correction, but may require further investigation
3.0 – 3.5mmol/L	If calcium has increased slowly, this may be tolerated but prompt treatment is usually indicated, especially if the patient is symptomatic
>3.5mmol/L	Severe hypercalcaemia with risk of dysrhythmia and coma

Adjusted calcium result may be invalid where albumin concentrations are very low (<15g/L) or high (>50g/L).

Urgent Action Required:

- **History, examination, ECG and bloods (details below)**
- **Rehydration**
  - **Intravenous 0.9% saline 4 – 6L in 24 hours[1]**
    - Tailor fluid therapy for individual patient, and review regularly
    - Monitor for fluid overload, especially in the elderly and patients with renal impairment or heart failure
    - Loop diuretics are not effective in lowering serum calcium – used rarely if fluid overload develops
    - Dialysis may need to be considered if severe renal failure is present
- **Further Treatment**
  If further treatment is required following IV saline, consider IV bisphosphonates[1*]
  - Zoledronic acid 4mg over 15min **OR**
  - Pamidronate 30 – 90mg (depending on severity of hypercalcaemia) at 20mg/h
  - Give more slowly and consider dose reduction if renal impairment is present
  - Monitor serum calcium – will reach nadir at 2 – 4 days
  - Can cause hypocalcaemia if vitamin D deficient or PTH is suppressed

*only licenced for hypercalcaemia in malignant conditions but can be considered off licence in severe refractory non-malignant cases

Further Investigations:

- History should include any symptoms and duration, as well as symptoms that may be attributed to an underlying cause e.g. weight loss
- Family history of hypercalcaemia should be noted
- Drug history should include over-the counter supplements and preparations containing calcium and vitamin D
- Examination should include assessment of cognitive function, fluid balance status and signs of an underlying cause
- ECG – in particular, look for shortened QT interval or other conduction abnormalities
- U&E, LFTs, and phosphate should be measured on serum (yellow top tube), and FBC and PTH on EDTA tubes. Note that 2 EDTA tubes are needed if FBC and PTH requested.
- Further investigations should be directed by the clinical situation, history, patient age etc, but may include serum and urine protein electrophoresis, vitamin D and urinary calcium. Contact the duty biochemist if you wish to discuss further.

Second line treatment and interpretation of results:

- Second line treatments include glucocorticoids, calcimimetics, denosumab, calcitonin and parathyroidectomy, but specialist advice should be sought if these are being considered

- Interpretation of biochemistry results:

    - A normal or raised PTH in the presence of hypercalcaemia indicates likely primary hyperparathyroidism (consider also tertiary hyperparathyroidism and familial hypocalciuric hypercalcaemia (FHH))
    - Patients with suspected primary hyperparathyroidism or FHH should be referred to endocrinology
    - A low PTH suggests a non-parathyroid cause e.g. malignancy, vitamin D intoxication and rarer causes (contact duty biochemist to discuss)

1. Walsh J, Gittoes N, Selby P, the Society for Endocrinology Clinical Committee. Society for Endocrinology Endocrine Emergency Guidance: Emergency management of acute hypercalcaemia in adult patients. Endocrine Connect 2016 vol 5, no. 5, G9-G11 published under Creative Commons 4.0 license (http://www.endocrineconnections.com/). Accepted for publication 3rd August 2016