Emergency management of acute hypercalcaemia in adult patients

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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 to rise. Serum calcium is bound to albumin, and measurements should be adjusted for serum albumin. This guideline aims to take the non-specialist through the initial phase of assessment and management.

Severity of hypercalcaemia

- <3.0 mmol/L: often asymptomatic and does not usually require urgent correction
- 3.0–3.5 mmol/L: may be well tolerated if it has risen slowly, but may be symptomatic and prompt treatment is usually indicated
- >3.5 mmol/L: requires urgent correction due to the risk of dysrhythmia and coma

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
- Familial hypocalciuric hypercalcaemia
- Non-malignant granulomatous disease
- Thyrotoxicosis
- Tertiary hyperparathyroidism
- Hypervitaminosis D
- Rhabdomyolysis
- Lithium
- Immobilisation
- Adrenal insufficiency
- Milk-alkali syndrome
- Hypervitaminosis A
- Theophylline toxicity
- 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 electrolytes

High calcium and high PTH = primary or tertiary hyperparathyroidism*
High calcium and low PTH = malignancy or other less common causes
(*Familial hypocalciuric hypercalcaemia may be misdiagnosed as primary hyperparathyroidism due to hypercalcaemia with inappropriately normal or raised PTH. However, the hypercalcaemia is not usually severe and it is less likely to present as an emergency)

Management

Rehydration

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

If further treatment required after intravenous saline, consider intravenous bisphosphonates

Zoledronic acid 4 mg over 15 min
OR Pamidronate 30–90 mg (depending on severity of hypercalcaemia) at 20 mg/h
OR Ibandronic acid 2–4 mg
- Give more slowly and consider dose reduction in renal impairment
- Monitor serum calcium response: will reach nadir at 2–4 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 40 mg daily
- Usually effective in 2–4 days

Calcimimetics, denosumab, calcitonin
- Under specialist supervision
- Can be considered if poor response to other measures

Parathyroidectomy
- Can be considered in acute presentation of primary hyperparathyroidism if severe hypercalcaemia and poor response to other measures

Disclaimer
The document should be considered as a guideline only; it is not intended to determine an absolute standard of medical care. The doctors concerned must make the management plan for an individual patient.

Sources
Emergency Guidance

J Walsh et al. Acute hypercalcaemia emergency guidance

Received in final form 3 August 2016
Accepted 3 August 2016

comparison of 30-, 60-, and 90mg doses. American Journal of Medicine 1993 95 297–304. (doi:10.1016/0002-9343(93)90282-T)


