

Hypercalcaemia in primary care

DEPARTMENT OF CLINICAL BIOCHEMISTRY



Severn Pathology

QPulse Reference: BS/CB/DCB/PROTOCOLS/39

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Version 6

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Definition

Mild
2.6 – 3.0mmol/L

Moderate
3.0 - 3.4mmol/L

Severe
> 3.4mmol/L

Adjusted Calcium
> 2.6 mmol/L (adjusted
for albumin), taken
without using a cuff

Symptoms/Clinical Signs

“Bones”
Bone pain or infrequently
fractures associated with an
underlying bone disorder

“Stones”
Polyuria, polydipsia, renal calculi

“Moans”
Fatigue, muscle weakness,
depression, confusion, coma

“Groans”
Nausea, vomiting, constipation,
pancreatitis, peptic ulcers

Hypercalcaemia
>3.0mmol/L can
potentiate cardiac
arrhythmias and is
often associated
with malignancy

Differential Diagnosis

90% of cases are either due to malignancy or
hyperparathyroidism
(in hospital 65% are due to malignancy)

1o Hyper-PTH

Incidence: 1-6 /1000
50-60yo
Female 5 : 1 Men
Benign in 80% of cases
Can be a part of MEN
syndromes

Familial Hypocalciuric Hypercalcaemia (FHH)

Benign condition
Autosomal Dominant
inheritance
High calcium,
high/normal PTH, low Ur
Calcium

Malignancy

Humoral hypercalcaemia of malignancy (80%)
PTH-related peptide (PTHrP) mediated
Lymphoma, Breast, SCLC, Head & Neck, Ovarian, Renal
cell

Lytic bone lesions (20%)

Multiple myeloma, Breast, Renal, Thyroid, Lung
cancers, rarely lymphoma & leukaemia

1, 25 (OH)₂ – Vit D
production

Lymphoma

Ectopic PTH

Ovarian, lung, thyroid,
rhabdomyosarcoma, pancreatic

Others

Medications, Renal Failure (3o hyper-PTH), Long-term
(e.g. ICU) immobilization, Granulomatous disease (Tb,
sarcoid), Addisons disease, Hyperthyroidism,
Pheochromocytoma

Initial investigations for hypercalcaemia

- Urea & Creatinine
- PTH
- 25(OH)-Vit D
- 1,25(OH)₂-Vit D if suspicion of granulomatous disease
- Urine sample for calcium/creatinine excretion ratio (CEI)
- Further investigations will be guided by history and examination (i.e. likelihood of malignancy or other rare causes)

Calcium Excretion index

- Fast the patient overnight.
- In the morning obtain the SECOND voided urine.
- Collect in universal/plain container.
- Request Calcium and Creatinine on urine sample.
- MUST be paired with a blood sample for Calcium and Creatinine.

The lab will calculate a calcium excretion ratio – a ratio of <22umol/L GF is likely to signify FHH where hypercalcaemia is present

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Hypercalcaemia confirmed (adjusted >2.6mmol/L)
Measure PTH

PTH < 1.6 pmol/L

Likely non-Parathyroid cause
Consider malignancy and the appropriate testing -> myeloma screen, PSA, breast exam, CXR or endocrine review

PTH >1.6pmol/L
Calcium >3.0mmol/L

Primary Hyperparathyroidism
Given degree of hypercalcaemia an urgent e-referral to endocrinology / contact on-call for immediate management advice

PTH mid ref range or higher (>approx4.5pmol/L)
Calcium 2.6-3.0mmol/L

Probable Primary Hyperparathyroidism
= Exclude Vit D deficiency – if VTD <50nmol/L, replace (not high dosing), then repeat in 2 weeks and reconsider PTH
= If still not suppressed and calcium <3.0mmol/L then consider calcium excretion ratio (2nd morning urine sample and serum sample for calcium and creatinine- see page 1)

Calcium excretion index low
(<22mmol/L GF)
FHH likely – refer to endocrinology

Calcium excretion index high
1o or 3o hyper-PTH likely - use referral criteria

Consider REMEDY guidelines under “Adults” -> “Endocrinology” for further guidance on primary hyperparathyroidism management

Refer to endocrinology if:
= <70 years old
= Ca >2.79mmol/L
= eGFR 30-44ml/min (CKD 3b)
= Symptomatic (incl renal stones)
= Hx of fracture or o’porosis

If not indicated to refer:
= Repeat calcium (not PTH) in 3 months and annually thereafter if stable
= Consider DEXA every 2-3 years
= If meet criteria at later stage then refer to endocrine

General Management considerations

<p><3.0mmol/L</p> <p>Review medications - Thiazide diuretics, Lithium, Calcium, Vit D, Vit A Review fluid status and rehydrate Consider admission if symptomatic</p>	<p>>3.0mmol/L</p> <p>Lower threshold for admission More likely to be significantly dehydrated and to need urgent investigation and ongoing biochemical monitoring -> contact endocrinology on-call directly</p>
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