

Hypercalcemia

Detected when

- Total S.Ca between 10.5 and 12 mg/ dL (2.63 and 3 mmol/ L) → Mild hypercalcemia
- >14 mg/ dL (3.5 mmol/ L) → Severe hypercalcemia⁵
- Or ionized Ca^{2+} >5.6mg/dl(1.4mmole/L)
- Or corrected Ca^{2+} > 10.5mg/dl(2.625mmole/L)

Take careful history and physical examination focusing on:

- 1-Clinical features of hypercalcemia (Bone pain, Arthritis, Osteoporosis, Renal stones, nausea, vomiting, muscle weakness, cardiac arrhythmia)
- 2-Possible causative diseases (Hyperparathyroidism, Malignancy, Vitamin D intoxication)
- 3-Possible causative medications, including OTC (Thiazide diuretics (usually mild), Lithium, calcium antacids, Vitamin A intoxication (including analogs used to treat acne) → Stop causative medications if possible, and recheck Ca level.

Measure intact PTH level, preferably with patient fasting repeat S.Ca level determination simultaneously

Low <10-65 pg/mL, 10-65 ng/L.

Clinical evaluation:

- Suspect malignancy→
- check for PTH-related protein syndromes
- Medications such as : Lithium, theophylline, tamoxifen
- Immobilization, Milk-alkali syndrome, Adrenal insufficiency, Hyperthyroidism

Evaluate and manage accordingly

Normal

Suspect Familial Hypocalciuric Hypercalcemia & +ve family history

Check 24-hr urine Ca conc. /CrCl

Ratio <0.01/ -ve family history

Normal

Treat as 1ry Hypercalcemia only

High >10-65 pg/mL, 10-65 ng/L.

1ry Hyperparathyroidism
(Consider Tc 99m sestamibi scan for accurate diagnosis)

Surgical treatment

If patient meets criteria:

- Symptomatic primary hyperparathyroidism (nephrolithiasis, nephrocalcinosis, osteitis fibrosa cystica)
- Asymptomatic :S.Ca level > 1.0 mg/ dL (0.25 mmol/ L) above the upper limits of normal
- Urinary Ca excretion > 400 mg /24 hrs (10 mmol/day)
- CrCl reduced by > 30% compared with age-matched persons
- Bone density (lumbar spine, hip, or forearm) that is > 2.5 standard deviations below peak bone mass (T score < -2.5)
- Patient age < 50 yrs, with asymptomatic 1ry hyperparathyroidism
- Medical surveillance not desirable or possible
- Surgery requested by patient

-Bisphosphonates for malignancy-related hypercalcemia. ZA is 100-850 times more potent than pamidronate and may be given as a bolus rather than an infusion.

Management

Non-pharmacological

*Patients with 1ry hyperparathyroidism → daily elemental Ca intake of 800-1000 mg & a vitamin D intake appropriate for their age and sex.
*Good hydration, regular exercise activity & avoidance of immobilization & certain medications (Diuretics esp thiazides, lithium)

Pharmacological

Look Algorithm 1ry Hypercalcemia

1ry Hypercalcemia

When all conditions mentioned above are negative

Adjuvant therapy

Glucocorticoids : Prednisone → 20-40 mg/day

Dialysis/haemofiltration → early stage in oligo-anuric renal failure / fluid overloaded.

Fluid volume

Dehydrated

Volume expansion with isotonic saline at an initial rate of 200 - 300 mL/hour → maintain the urine output at 100 - 150 mL/hour

Overload

Calciuresis after intravascular volume repletion, a forced diuresis with furosemide +0.9% saline (6-8L/d). An effect seen within 12h. **(Thiazides should not be used)**

Salmon calcitonin 4 IU/kg/12 hrs IM/SC if response unsatisfactory after 24-48 hrs → increase to 8 IU/kg/12 hrs up to max. 8 IU/Kg/6hrs OR 100 IU/6-8hrs increased after 1-2days to max.400 IU/6-8hrs
In crisis given IV 10 IU/Kg diluted in 500ml Saline as slow infusion over at least 6 hrs.
Its action is usually short-lived and rebound hypercalcaemia may occur

Bisphosphonates (e.g. pamidronate) and IV PO4 should only be given after specialist advice is taken in view of their toxicity and potential complications →ZA; 4 mg [IV] over 15 mins or Pamidronate (60-90 mg over 2 hrs) or Ibandronate doses of 2 mg IV over 2 hrs normalized S.Ca, doses up to 6 mg were safe.

Contraindicated

Denosumab → 120 mg SC/ 4 weeks → additional 120 mg doses on Days 8 and 15 of the 1st month of therapy

Dose Adjustments of ZA

Nononcology uses:

CrCl 35 to 80 mL/minute → No dose adj. CrCl <35 mL/minute → contraindicated.

Oncology uses:

Multiple myeloma and bone metastases:

CrCl >60 mL/min: 4 mg (no dose adj.) CrCl 50-60 mL/min → dose 3.5 mg

CrCl 40-49 mL/min → dose 3.3 mg CrCl 30-39 mL/min → dose 3 mg

CrCl <30 mL/min → Not recommended.

Hypercalcemia of malignancy:

-Mild to moderate impairment → No dose adj.

-Severe impairment (S.Cr >4.5 mg/dL): Evaluate risk VS benefit

Dose adj. for renal toxicity during ZA ttt:

-Hypercalcemia of malignancy: Evidence of renal deterioration: Evaluate risk VS benefit.

-MM → withheld for deterioration in renal function (increase of S.Cr ≥0.5 mg/dL in patients with normal baseline S.Cr or increase of ≥1 mg/dL in abnormal baseline S.Cr). Reinitiate at the same dose when S.Cr returns to within 10% of baseline.

-Albuminuria >500 mg/24 hrs(unexplained): Withhold dose until return to baseline, then reevaluate /3-4 weeks; consider reinitiating with a longer infusion time of 30 mins or longer.

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