

Palliative Care Tip – Issue#7:
HYPERCALCEMIA OF MALIGNANCY / June, 2018

Definition: Hypercalcemia (HyperCa⁺⁺) = corrected Ca⁺⁺>2.60 mmol/L

N.B.: corrected serum calcium = measured serum calcium + {(40 – measured serum albumin) x 0.02}

Causes:

- Occurs 20-30 % of cases in advanced cancer (solid and hematological) related to humoral hyperCa⁺⁺, local release of cytokines, induced by 1,25-dihydroxyvitamin D, but most commonly by production of parathyroid hormone-related peptide (PT-HRP).
- Most commonly occurs in breast cancer, renal cell carcinomas, and squamous cell carcinomas.
- Less often related to increased gastrointestinal absorption of calcium or ectopic production of PTH itself.

Clinical Features:

- Can be severe, difficult to manage and often presents insidiously
- Symptoms are often difficult to distinguish from those related to the underlying malignancy.
- Lethargy, anorexia, nausea, vomiting, thirst, polydipsia, constipation, dehydration.
- Cognitive difficulties, confusion, obtundation, and coma may occur.

Treatment:

Mild to moderate HyperCa⁺⁺ and minimal symptoms:

- a) Rehydrate (Normal Saline; hypodermoclysis [HDC] at 100 mL/hr or IV at 100-120 mL/hr).
 - b) Recheck serum calcium in 24-48 hours – if HyperCa⁺⁺ persists, consider a bisphosphonate (see below).
- Severe HyperCa⁺⁺ (corrected serum Ca⁺⁺>3.0 – 3.5 mmol/L) and/or very symptomatic:*
- a) First, rehydrate (Normal saline HDC at 100 mL/hr or IV at 100-300 mL/hr).
 - b) If renal function is normal, administer a bisphosphonates (see below) while hydrating.
 - c) In the absence of renal failure or heart failure, avoid loop diuretics because of potential complications
 - d) If renal function is impaired, hydrate first (as above), to correct pre-renal failure and consider administering Calcitonin (100-200 units subcut TID x 3-6 doses) to bridge to administration of a bisphosphonate. Consider this if symptoms are severe, and HyperCa⁺⁺ must be corrected quickly. (note: calcitonin's anti-hyperCa⁺⁺ effect diminishes in 24-48 hours).
 - e) Recheck serum calcium 3-4 days following bisphosphonate administration.

Bisphosphonates:

- Renal failure is a relative contraindication to use of bisphosphonates, therefore, check electrolytes, urea and creatinine prior to administration. If pre-renal failure is present, rehydrate prior to use.

Pamidronate – duration of effect 28 days

- Limitation: cannot be given subcutaneously.
- Cheapest of all the bisphosphonates
- Dose: Pamidronate 60-90 mg (if renal function normal, 90mg recommended) in 500-1000 mL NS or D5W to run over 4-6 hrs, intravenously.

Clodronate – duration of effect 14 days

- Limitation: access has become limited, please check with local pharmacies/hospitals for availability
- If available, can be administered subcut. permitting home administration (monitor site for irritation)
- Dose: Clodronate 1500 mg subcut or IV in 500-1000 mL NS or D5W to run over 4-6 hrs.

EDMONTON ZONE – PALLIATIVE AND END OF LIFE CARE

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Zoledronic Acid – duration of effect 4 weeks

- Limitation: Intravenous route only
- 4 mg intravenously over 15 min. Superior to pamidronate in reversing HyperCa⁺⁺ related malignancy.
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Denosumab – duration of effect 4 weeks

- For severe, symptomatic HyperCa⁺⁺ related malignancy, refractory cases to zoledronic acid.
- *60 mg subcut with repeated dosing based on response or 120mg subcut, (cost may be lifted factor especially outpatient setting).*

Special Notes

- While treating the HyperCa⁺⁺ is a priority, also ensure symptoms resulting from it (agitation, restlessness, constipation) are symptomatically managed as well.
- If further concern for symptom management, consider consulting the Palliative Care Program (see Issue #23).