

HYPERCALCEMIA

(Last updated 01/10/2020; Last reviewed 03/11/2017; Reviewers: Rudy Tedja, DO, Bibek Karki, MBBS)

PRESENTING COMPLAINT: Weakness, fatigue, constipation, depression

FINDINGS

- **A** Check airway
- **B** ↓/N RR
- **C** ↑/N BP, ↓HR
- **D** Variable altered (V,P,U,D)*
- **E** Profound muscle weakness, bone pain
- **L_{PC}** ↑Ca, ↑/↓/N PTH, ↑/↓/N P
- **U_{PC}** Renal stone

***V** (verbal), **P** (pain), **U** (unconsciousness), **D** (delirious)

U_{PC} (point of care ultrasound) **L_{PC}** (point of care labs)

OTHER HISTORY

Signs and symptoms

- Neurological: Lethargy, confusion, stupor, coma
- Cardiac: Shortened QT interval, supraventricular, ventricular arrhythmias, bradycardia
- Renal: Polyuria, nephrolithiasis, nephrogenic diabetes insipidus, renal insufficiency, renal tubular acidosis
- MSK: Bone pain
- GI: Nausea/vomiting, abdominal pain, pancreatitis

Predisposing Conditions: Elderly are predisposed to neuropsychiatric symptoms and known history of malignancy

DIFFERENTIAL DIAGNOSIS

Other causes of drug induced or metabolic encephalopathy/coma, delirium, intracranial pathology

OTHER INVESTIGATIONS

- **Lab:** Creatinine
- **Severity:** Mild: Calcium < 12 mg/dL; moderate: Calcium 12-14 mg/dL; severe: Calcium >14 mg/dL
- **Monitoring:** Calcium level every 8 hours

THERAPEUTIC INTERVENTIONS

- **Initial therapy**

- Stop any offending agents, such as thiazides, lithium, exogenous calcium, vitamin A supplementation, vitamin D supplementation
 - Intravascular volume repletion with isotonic saline at initial rate of 200-300 ml/hr
 - Depending on renal function and history of CHF
 - Titrate rate of normal saline to goal urine output of 100-150 ml/hr
 - Calcitonin at 4-8 IU/kg IM or SQ q12 hr x 48 hr: Effective within 4-6 hr of administration
 - Bisphosphonates: Zoledronic acid at 4 mg IV over 15 min or pamidronate at 60-90 mg over two hours, Bisphosphonate will be effective 2nd-4th day
 - Dialysis may be required in patients that have oligo/anuric AKI, advanced chronic kidney disease, or CHF where aggressive fluid resuscitation is contra-indicated
 - Once euvolemia is restored, administration of **loop diuretics** to enhance calciuresis is indicated
- **Consult:** Nephrology, endocrinology

MANAGEMENT AFTER STABILIZATION

- Differentiate between parathyroid hormone (PTH)- mediated hypercalcemia and non-PTH-mediated:
 - PTH mediated: Hyperparathyroidism
 - Non-PTH mediated: Malignancy (Especially multiple myeloma), vitamin A and D toxicity, sarcoidosis, milk-alkali syndrome, paget's disease, familial hypocalciuric hypercalcemia, adynamic bone disease, hyperthyroidism, adrenal insufficiency, drugs (thiazides, lithium)
- **Additional labs if non-PTH mediated:** PTH-related peptide, 1,25 OH vitamin D, vitamin A level, serum free light chains, UPEP, 24-hr urine calcium, TSH, cortisol
- **Follow up:** Goal is to prevent recurrence of hypercalcemia; Monitor serum calcium level every 4 hours
- **Further treatment:** Patients with malignancy and metastatic bone disease needs bisphosphonate every 3-4 weeks; For patients with malignancy, treat the underlying malignancy
- **Prophylaxis:** See above for prevention

CAUTIONS

- **Complications:** Watch for volume overload during saline hydration: Particularly in patients with renal failure or heart failure
- **Manage complications:** Furosemide for volume-overloaded patients, Electrolyte imbalance from furosemide-induced diuresis

REFERENCES & ACKNOWLEDGEMENTS

Acknowledgement: *Gina Iacovella, MD*

- Major, P., et al., Zoledronic acid is superior to pamidronate in the treatment of hypercalcemia of malignancy: a pooled analysis of two randomized, controlled clinical trials. *Journal of Clinical Oncology*, 2001. **19**(2): p. 558-567.
- LeGrand, S.B., D. Leskuski, and I. Zama, Narrative review: furosemide for hypercalcemia: an unproven yet common practice. *Annals of internal medicine*, 2008. **149**(4): p. 259-263.
- Uptodate