## Usual Treatment

- Aldosterone antagonists, such as spironolactone (up to 300 mg/d) or the newer drug eplerenone (up to 100 mg/d).
- Both spironolactone and eplerenone are mineralocorticoid receptor antagonists and therefore have a potassium-sparing diuretic effect. Eplerenone is more selective for the mineralocorticoid receptor than spironolactone and has fewer glucocorticoid or androgen receptor antagonist side effects.
- Htn may be refractory to treatment with aldosterone antagonist alone and may require formal antihypertensive therapy with ACE inhibitor or beta-blocker.
- Treatment of Htn may be needed for several wk before any benefit to periop morbidity.
- Assess volume status thoroughly; there may be occult hypovolemia if diuretic treatment has been started.
- Hypervolemia should be treated with a potassium-sparing diuretic such as amiloride to avoid exacerbating potassium loss.
- Potassium deficit is likely to be severe and larger than apparent from serum levels.

## Assessment Points

| System | Effect | Assessment by Hx | PE | Test |
|---|---|---|---|---|
| CV | Htn, often resistant to therapy; increased sympathetic activity, cardiac output often decreased even in absence of Htn. May have unexplained congestive failure | Exercise tolerance, dyspnea, orthopnea, Htn-headache, visual disturbance | BP (compare R to L or arms with legs with coarctation)<br>Third heart sound<br>Fine inspiratory crackle<br>Oedema | BP, ECG, ABG, CXR, ECHO |
| HEME | Hypervolemia or hypovolemia (or decreased plasma volume in edematous states) may result in Htn or hypotension, hypokalemia, metabolic acidosis | Syncope, weakness, fatigue | JVP, postural BP, motor power | Serum electrolytes, bicarbonate, ABG |
| RENAL | Increased renal tubular sodium absorption<br>Azotemia may be caused by decreased renal perfusion or ineffective plasma volume. In setting of renal artery stenosis, ACE inhibitors may exacerbate renal failure; hypokalemia, alkalosis | Htn, decreased urine output, chronic renal disease, weakness | Abdominal bruit suggests renal artery stenosis<br>Edema | ECG, serum and urine lytes, ABG, abdominal ultrasound with renal artery Doppler or contrast CT imaging, renal biopsy. |
| HEPAT | Cirrhosis is an edematous state and may be associated with occult hypovolemia, altered pharmacokinetics, hypoalbuminemia, coagulopathy, encephalopathy, variceal bleeding risk | Alcohol excess, hepatitis, other liver disease, bruising after minor injury. | Pallor, jaundice, ascites, asterixis ephalopathy, porto-systemic anastomoses, bruising, hepatomegaly | Full blood count including coagulation studies and platelets, serum lytes, hepatic enzymes, bilirubin, ammonia, abdominal ultrasound, liver biopsy |

**Key References:** Davies M, Hardman JG: Anaesthesia and adrenocortical disease, *Contin Educ Anaesth Crit Care Pain* 5(4):122–126, 2005; Reilly CS: Adrenal disease: cortex and medulla. In Hall GM, Hunter JM, Cooper MS, editors: *Core topics in endocrinology in anaesthesia and critical care*, Cambridge, 2010, Cambridge University Press, pp 45–56.

## Perioperative Implications

### Preinduction/Induction/Maintenance

- Dependent on primary underlying medical problem causing increased renin secretion.
- Assess cardiac function and circulating volume status to guide choice of induction agent; beware of altered pharmacokinetics; anticipate severe cardiovascular instability.
- Correct hypokalemia and associated electrolyte disturbance (e.g., magnesium); this may require IV supplementation preop and intraop.
- Htn may be refractory; require treatment with several classes of drugs with the potential for extreme cardiovascular instability. There may be a disproportionate hypertensive response to laryngoscopy or surgical stimulation.
- Avoid hyperventilation and hypocapnia to prevent worsening metabolic alkalemia and subsequent intracellular potassium shift.
- Anticipate increased sensitivity to nondepolarizing neuromuscular antagonists due to hypokalemia. Consider using drugs with spontaneous organ independent metabolism (e.g., atracurium or cisatracurium, or rocuronium and sugammadex combination).

### Monitoring

- Consider arterial pressure monitoring.
- Consider central venous cath insertion for access and administration of concentrated potassium and magnesium in the face of hypervolemia, or for monitoring filling pressure where there is cardiomyopathy and heart failure.
- Urinary cath.
- Peripheral nerve stimulation for neuromuscular function.

### General Anesthesia

- Consider underlying and associated underlying medical comorbidities.
- Hypokalemia may potentiate muscle relaxants and arrhythmia.
- High pH decreases availability of intracellular calcium.

### Regional Anesthesia

- Pt with severe edema may be unable to tolerate supine operating positions while awake.
- Local anesthetic mixtures with sympathomimetic may exacerbate preexisting Htn.
- Altered pharmacokinetics resulting from hypervolemia, edema, and end organ damage such as hepatic and renal dysfunction may need dose adjustments.

### Postoperative Period

- Appropriate care predicated on surgical procedure, comorbidities, and hemodynamic stability.
- Monitor and correct ongoing electrolyte abnormalities.
- Altered pharmacokinetics may be associated with prolonged recovery times from anesthetic agents and exaggerated response to opioid analgesia.

## Anticipated Problems/Concerns

- Labile BP
- Pts with preexisting Htn, left ventricular hypertrophy, and cardiac failure are at increased risk of morbidity and mortality from stroke and MI.
- Increased sympathetic activity leads to further activation of the renin-angiotensin system.
- Arrhythmia from severe hypokalemia.
- Generalized muscle weakness from hypokalemia.

# Hypercalcemia

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## Perioperative Risks

- Pts with normal renal and CV function who have moderate hypercalcemia (11.5–13 mg/dL) have no special preop problems but may exhibit lethargy, anorexia, nausea, and polyuria.
- Lithium and thiazide diuretics should be held.
- Severe hypercalcemia (>13 mg/dL) carries risk for hypovolemia and acid-base abnormalities; therefore, normal intravascular volume and electrolyte status should be restored prior to surgery.
  - Neuromuscular symptoms may occur with associated muscle weakness.
  - Neurologic disturbances ranging from poor concentration to coma can develop.
  - CV effects include Htn, dysrhythmias, heart block, ST segment elevation mimicking MI, cardiac arrest, and digitalis sensitivity.
- Total serum $Ca^{2+}$ >14 mg/dL is a medical emergency and requires immediate treatment and delay of elective surgical procedures.

## Worry About

- Volume status (hypovolemia secondary to polyuria, fluid overload secondary to treatment).
- Electrolyte disturbances.
- Dysrhythmias and/or ECG changes.
- Organ system manifestations of hypercalcemia and underlying disease.
- Longstanding hypercalcemia can lead to calcification in the myocardium, blood vessels, brain, and kidneys. Beware of seizures from cerebral calcifications. Polyuria that is unresponsive to vasopressin may result from renal calcifications.

## Overview

- Total body $Ca^{2+}$ is stored in bone (99%) and serum (1%).
- Total serum $Ca^{2+}$ exists in three fractions: 50% protein-bound (mainly to albumin), 40–50% free or ionized (the physiologically active fraction), and 5–10% anion-bound (to phosphate or citrate).
- The normal range for total serum calcium is 8.6–10.4 mg/dL; the normal range for ionized calcium is 4.7–5.3 mg/dL. Hypercalcemia is defined as total serum $Ca^{2+}$ >10.4 mg/dL.
- The total serum $Ca^{2+}$ level should be corrected for serum albumin level; for every 1 mg/dL decrease in serum albumin, there is a 0.8 mg/dL increase in $Ca^{2+}$.
- Normal serum $Ca^{2+}$ is regulated by several factors:
  - PTH, which increases bone resorption and renal tubular resorption of calcium.
  - Calcitonin, which inhibits bone resorption.
  - Vitamin D, which augments intestinal absorption of $Ca^{2+}$.

## Etiology

- Increased resorption of calcium from bone (primary/secondary hyperparathyroidism, malignancy, hyperthyroidism, administration of estrogen or antiestrogens to breast cancer pts), with breast cancer accounting for 25–50% of malignancy-related hypercalcemia
- Increased absorption from GI tract (granulomatous diseases such as sarcoidosis, vitamin D intoxication, milk-alkali syndrome)
- Decreased renal excretion of calcium (thiazide diuretics, lithium therapy, familial hypocalciuric hypercalcemia, and renal insufficiency)

## Usual Treatment

- Initiated in pts with total serum $Ca^{2+}$ >14 mg/dL or symptomatic pts with total serum $Ca^{2+}$ <14 mg/dL.
- Volume expansion with saline to correct fluid deficit (from polyuria) and increase urinary excretion of $Ca^{2+}$.
- Loop diuretics increase urinary excretion of sodium and $Ca^{2+}$ with avoidance of thiazide diuretics.
- Discontinue offending drugs, implement dietary $Ca^{2+}$ restriction, and encourage increased physical activity.
- Calcitonin, bisphosphonates, or mithramycin may be required in disorders associated with osteoclastic bone resorption.
- Hydrocortisone may be used to reduce GI absorption of $Ca^{2+}$ in granulomatous disease, vitamin D intoxication, lymphoma, and myeloma. Hydrocortisone is not helpful in pts with hypercalcemia due to hyperparathyroidism or other malignancies.
- Dialysis may be required for life-threatening hypercalcemia.
- Surgical removal of the parathyroid glands can treat primary or secondary hyperparathyroidism.
- Treat underlying cause.

## Assessment Points

| System | Effect | Assessment by Hx | PE | Test |
|---|---|---|---|---|
| CV | Hypovolemia<br>Shortening of the Q-T interval, prolonged P-R intervals, wide QRS complexes, bradycardia<br>Htn | Postural symptoms<br>Palpitations, fatigue, poor exercise tolerance, dizziness, syncope<br>Headache | Orthostatic vital signs, narrowed pulse pressure, tachycardia<br>Auscultation, variable or slow heart rate<br>Elevated BP | ECG |
| NEURO | Decreased concentration, confusion, fatigue, stupor and/or coma, seizure (rare) | Confusion<br>Obtundation and/or coma | Mini-mental exam | EEG |
| RENAL | Polyuria; polydipsia; renal tubular acidosis; nephrogenic diabetes insipidus<br>Nephrolithiasis; nephrocalcinosis<br>Acute and chronic renal insufficiency | Increased frequency of urination, excessive thirst, lithium use, abd pain<br>Low urine output | Signs of dehydration (dry mucous membranes, poor capillary refill, decreased skin turgor)<br>Flank pain | Lytes, BUN, Cr, UA urinalysis<br>Abdominal x-ray or CT |
| MS | Muscle weakness<br>Lytic bone lesions<br>Osteopenia and/or osteoporosis | Muscle weakness<br>Bone pain | Decreased muscle strength and tone, depressed deep tendon reflexes<br>Pain on palpation or limited ROM | X-ray (lytic lesions or pathologic fracture)<br>DXA |
| ENDO | Excess PTH or production of PTH-related hormone | | | Radioimmunoassay of PTH or PTH-related peptides |
| GI | Anorexia, nausea and/or vomiting, bowel hypomotility and constipation, pancreatitis<br>PUD | Poor appetite, nausea and/or vomiting, constipation, abd pain<br>GI bleeding | Abdominal pain | Abdominal x-ray or CT scan, colonoscopy, LFTs (amylase and lipase)<br>EGD |

**Key References:** Shane E, Dinaz I: Hypercalcemia: pathogenesis, clinical manifestations, differential diagnosis, and management. In Favus MJ, editor: *Primer on the metabolic bone diseases and disorders of mineral metabolism*, ed 6, Philadelphia, PA, 2006, Lippincott Williams and Wilkins; Nishi SP, Barbagelata NA, Atar S, Birnbaum Y, Tuero E: Hypercalcemia-induced ST-segment elevation mimicking acute myocardial infarction, *J Electrocardiol* 39(3):298–300, 2006.

## Perioperative Implications

### Preinduction

- Acquire knowledge of and treat the underlying cause.
- Determine if the hypercalcemia is acute or chronic.
- Assess volume status: Hydrate to attain normal intravascular volume and to promote renal excretion of $Ca^{2+}$.
- Administer diuretics (loop diuretics, as thiazides increase reabsorption of calcium) to increase urinary $Ca^{2+}$ excretion if serum $Ca^{2+}$ >14 mg/dL.
- Correct other electrolyte imbalances, including hypophosphatemia, hypokalemia, and hypomagnesemia.

### Induction

- No specific anesthetic drug or technique has advantages in a pt with hypercalcemia; however, hemodynamic instability may occur if standard dosing is used in a hypovolemic pt.

### Monitoring

- Standard ASA monitors +/– CVP monitoring.
- Volume status (urine output and fluid administration); depending on the severity of hypercalcemia, underlying cause, the pt's CV status, and type of surgery, additional monitors of volume status (CVP or TEE) should be considered.
- Lytes (venous or arterial).
- 5-lead ECG to monitor for shortened Q-T interval, S-T changes, decreased T wave amplitude, or T wave inversion.
- BP to monitor for Htn; approximately one-third of hypercalcemic pts have Htn that usually resolves with treatment of the primary disease.

### General Anesthesia/Maintenance

- Routine maintenance tailored to the comorbidities of the pt and the surgical needs.
- Continued hydration and electrolyte replenishment to attain normal intravascular and acid-base status.
- Hypercalcemia may be associated with decreased sensitivity to muscle relaxants and thus a shortened time course of neuromuscular blockade; however, associated electrolyte disturbances or renal insufficiency may prolong neuromuscular blockade.
- Careful positioning of the anesthetized pt is important because osteopenia/lytic bone lesions predispose these pts to pathologic bone fractures.
- If the pt is mechanically ventilated, avoid resp alkalosis because alkalosis lowers plasma $K^+$, which would leave hypercalcemia unopposed.

### Regional Anesthesia

- General anesthesia is most commonly used for parathyroid surgery; however, a cervical plexus block or local anesthesia with hypnosis has also been used.

### Postoperative Period

- Continue to monitor the same intraop parameters, with continued close attention to volume status.
- Hypercalcemia, hypermagnesemia, and hyponatremia are rare causes of delayed emergence.
- After parathyroid surgery, monitor for bleeding, recurrent laryngeal nerve injury or hypocalcemia (secondary to profound decrease in PTH).

## Anticipated Problems/Concerns

- Fluid and electrolyte disturbances: Correct $Mg^{2+}$, phosphate, and $K^+$ levels in the periop period, as they may be altered with the treatment of hypercalcemia.
- Acute ECG changes and arrhythmias.
- Neurologic impairment: As $Ca^{2+}$ increases, the worsening mental status may lead to impaired airway protection.
- When hypercalcemia is severe and/or the pt is symptomatic, do not hesitate to consult a specialist (endocrinologist, nephrologist, or cardiologist) and postpone surgery if possible.