

# Hyperparathyroidism

Hyperparathyroidism is present when secretion of PTH is increased (primary hyperparathyroidism) Secondary hyperparathyroidism reflects an appropriate compensatory response of the parathyroid glands to secrete more parathormone to counteract a disease process that produces hypocalcemia, it seldom produces hypercalcemia. Ectopic Hyperparathyroidism (Pseudohyperparathyroidism) is a paraneoplastic syndrome of PTH (or similar protein) secretion. PTH stimulates bone resorption, inhibits renal excretion of calcium, and increases conversion to active vitamin D. The net effects of increased PTH are: Increased Calcium, Increased Vitamin D, and Decreased PO4. Symptoms of Hyperparathyroidism are related to hypercalcemia. Hypercalcemia (serum calcium concentration >5.5 mEq/L and ionized calcium concentration >2.5 mEq/L) is the hallmark of primary hyperparathyroidism.

## ANESTHETIC CONSIDERATIONS PATIENT:

- Hypercalcemia:
  - Hypertension
  - Possible intravascular volume depletion (diuresis)
  - CVS Calcification: Valves, Coronary Arteries, Myocardial Fibres
  - Psychiatric Disturbances: Anxiety, Depression, Cognitive Dysfunction, Psychosis
  - Renal Disease: Renal Failure, Stones, Nephrogenic DI
  - Muscle and Bone Weakness
  - Possible decreased pain sensation
  - Unpredictable response to muscle relaxants
- Etiology and underlying condition:
  - Risk of MEN I and MEN IIa (phea)
  - Possible Paraneoplastic Secretion - Carcinoma of the lung, breast, pancreas, or kidney and lymphoproliferative disease

## ANESTHETIC CONSIDERATION PROCEDURE:

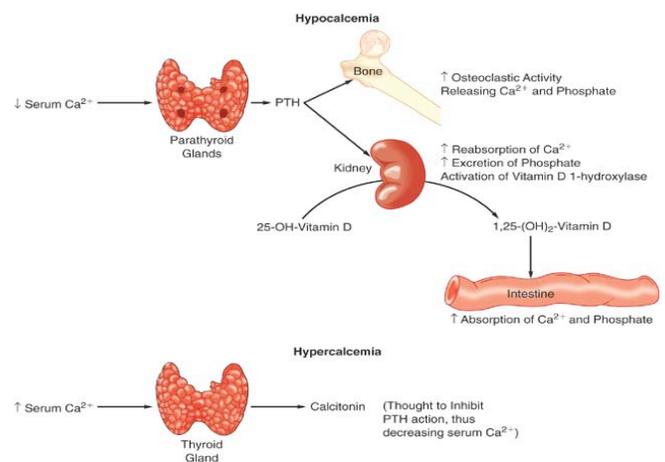
- Shared airway
- Post-op Airway Compromise (Recurrent laryngeal nerve injury, Hematoma, Hypocalcemia)
- Transient or complete hypoparathyroidism and hypocalcemia
- “Hungry bone” syndrome

## ANESTHETIC GOALS:

- Preoperative optimization:
  - Delay elective or non-urgent cases until calcium levels are normalized
  - Rehydrate and ensure adequate urine output pre-operatively and intra-operatively
  - Stress Dose of Steroids if Patient treated with same
- Careful patient positioning – risk of fractures
- Avoid psychotropic drugs (ex. Ketamine) in patients with psychiatric disturbances
- Avoid Nephrotoxic Drugs and adjust for dosage for renally excreted drugs
- Careful titration of NMBAs and monitor using a peripheral nerve stimulator.
- Avoid Acidosis - Possible Benefit of Mild Hyperventilation (respiratory alkalosis lowers iCa)
- Monitor for Post-op Airway Compromise (bleeding, recurrent laryngeal nerve injury, hypocalcemia)

## ETIOLOGY AND PATHOPHYSIOLOGY

- PTH Homeostasis
  - PTH secretion increased by:
    - Low Calcium
    - Low Magnesium
  - Increased PTH causes: Increased ECF Calcium and Vitamin D
    - Bone – Release of Calcium and Phosphate by:
      - Increased Osteoclast Activity
      - Increased Bone Resorption
    - Kidney
      - Phosphate and bicarbonate excretion and decreased reabsorption
      - Calcium and Magnesium Resorption
      - Increased 1-alpha-hydroxylase activity
  - Increased PTH causes Increased Calcium, Increased Vitamin D, and Decreased PO4
- Vitamin D Causes Increased Calcium and Increased PO4
- Causes of Hypercalcemia (Not Necessarily High PTH):
  - GRIM ED: Granulomas (Sarcoid, TB), Renal Failure, Immobility, Malignancy (metastatic disease, multiple myeloma), Endocrine (Hyperparathyroidism, hyperthyroidism, adrenal insufficiency), Drugs (Thiazides and Lithium)
  - Transient hypercalcemia may follow otherwise successful renal transplantation
  - Milk alkali syndrome, Vitamin D intoxication, Paget's disease
  - Albumin
    - In general, an increase or decrease in albumin of 1 g/dL is associated with a parallel change in total serum Ca<sup>2+</sup> of 0.8 mg/dL
    - Acidosis decreases protein binding (increases ionized Ca<sup>2+</sup>)
- Primary Hyperparathyroidism
  - Primary hyperparathyroidism occurs in about 0.1% of the population
  - Most commonly begins in the third to fifth decades of life
  - Occurs two to three times more frequently in women than men.
  - Results from excessive secretion of parathormone due to:
    - Benign parathyroid adenoma (90%)
    - Carcinoma of a parathyroid gland (5%)



- MEN I – Werner’s Syndrome
    - Pituitary Adenoma (May secrete GH and Prolactin, may be non-secretatory)
    - Primary Hyperparathyroidism
    - Entero-pancreatic endocrine tumor
      - Insulinoma (hypoglycaemia)
      - Gastrinoma (PUD)
      - VIPomas (secretory diarrhea)
      - Pancreatic islet cells tumors
    - Hyperparathyroidism due to an adenoma or hyperplasia is the most common presenting symptom of multiple endocrine neoplasia 1 syndrome.
    - Hyperparathyroidism has 100% penetrance by 40 to 50 years of age with MEN I
  - MEN IIa – Sipple’s Syndrome
    - Medullary Thyroid Carcinoma (>90%)
    - Pheochromocytoma (40-50%)
    - Hyperparathyroidism (10-20%)
    - Cutaneous Lichen Amyloidosis)
  - MEN IIb does not exhibit hyperparathyroidism
    - Hyperplasia of the parathyroid glands - usually involves all four parathyroid glands
  - Modest increases in plasma calcium concentrations discovered incidentally in otherwise asymptomatic patients are most likely due to parathyroid adenomas, whereas marked hypercalcemia (>□7.5 mEq/L) is more likely due to cancer
  - Secondary hyperparathyroidism
    - Reflects an appropriate compensatory response of the parathyroid glands to secrete more parathormone to counteract a disease process that produces hypocalcemia
    - Seldom produces hypercalcemia
    - Treat underlying disorder
    - Chronic renal disease is a common cause of hyperphosphatemia (due to decreased phosphate excretion) and decreased vitamin D metabolism. The hypocalcemia that results leads to an increased production of PTH
  - Tertiary hyperparathyroidism
    - development of hypercalcemia in a patient who has had prolonged secondary hyperparathyroidism that has caused adenomatous changes in the parathyroid gland and unregulated PTH
  - Ectopic hyperparathyroidism (humoral hypercalcemia of malignancy, pseudohyperparathyroidism)
    - Due to secretion of parathormone (or a substance with similar endocrine effects) by tissues other than the parathyroid glands
    - Carcinoma of the lung, breast, pancreas, or kidney and lymphoproliferative disease are the most likely ectopic sites for parathormone secretion
- Associated with anemia and increased plasma alkaline phosphatase concentrations **HISTORY**
- Symptoms of Hypercalcemia:
    - “Bones, Stones, Moans, Groans, Psychiatric overtones”
    - Primary Hyperparathyroidism is usually less symptomatic than hypercalcemia from cancer

#### SYSTEM BASED CONSIDERATIONS

- Airway
  - Aspiration Risk (vomiting)
  - Post-op Airway Compromise (Recurrent laryngeal nerve injury, Hematoma, Hypocalcemia – laryngospasm, bronchospasm)
  - Rarely, the parathyroid glands can become so enlarged that they compromise the airway
- Breathing/Respiratory
  - Decreased clearance of secretions from the tracheobronchial tree → postop atelectasis
- CVS
  - Hypertension
  - Arrhythmia – bradycardia, heart block, bundle branch block
  - Calcium deposition on valves, coronary arteries and myocardial fibres
  - Anemia
  - Intravascular volume depletion (may have hypotension)
  - Hypophosphatemia can impair myocardial contractility
- Neuro
  - Hypotonia, Hyporeflexia, Paresis
  - Reversible Skeletal Muscle Neuropathy (reversible)
  - Cerebral calcifications may cause seizures
- GI
  - Constipation, Anorexia, N+V, PUD, Pancreatitis, abdominal pain (may mimic acute abdomen)
- GU
  - Polyuria, Polydipsia, Nephrogenic DI, Kidney Stones, Renal Failure
  - Renal calcifications lead to polyuria that is unresponsive to vasopressin.
- Other
  - Hypercalcemia
  - Bone
    - Pain, Pathologic Fractures, Vertebral collapse, osteitis fibrosa cystica
  - Weakness
  - Psychiatric Disturbances: Anxiety, Cognitive Dysfunction, Psychosis
  - Metabolic Acidosis
  - Loss of sensation for pain and vibration may occur.
- Pregnancy
  - Primary hyperparathyroidism occurring during pregnancy is associated with a high maternal and fetal morbidity rate (50%).
  - The placenta allows the fetus to concentrate calcium, promoting fetal hypercalcemia and leading to hypoparathyroidism in the newborn.
  - Pregnant women with primary hyperparathyroidism should generally be treated with surgery.

#### DRUGS

- Avoid ketamine in patients with psychiatric disturbances
- Potential risk of sevoflurane in patients with renal dysfunction

- Unpredictable response to muscle relaxants
  - Monitor the response using a peripheral nerve stimulator.
- Thiazide diuretics should be avoided as they increase renal tubular reabsorption of calcium
- Increased sensitivity to digitalis
- Resistance to catecholamines.
- Propofol can interfere with the PTH assay,
  - many surgeons prefer that propofol not be used within 15 minutes of an assay

#### INVESTIGATIONS

- Calcium
  - Ionized calcium:
    - physiologically active form of calcium
    - represents approximately 45% of the total serum calcium concentration.
    - Dependent on arterial pH and the plasma albumin concentration
- PTH, Magnesium, PO<sub>4</sub>
- CBC, electrolytes, Creatinine, Urea
- ABG – check for metabolic acidosis
- Urinary excretion of cyclic adenosine monophosphate is increased in patients with primary hyperparathyroidism
- ECG: Short QT, Prolonged PR interval, Arrhythmia.
  - Severe hypercalcemia (e.g., total serum Ca<sup>2+</sup> >15 mg/dL) causes a decrease in T-wave amplitude or T-wave inversion
  - May produce a high-takeoff ST segment in leads V<sub>1</sub> and V<sub>2</sub> simulating acute ischemia
- Investigations for MEN I and MEN IIa (esp. pheo)

#### TREATMENT

- Medical Management
  - Decrease GI Calcium Absorption
    - Oral Phosphates
    - Hydrocortisone
      - may reduce gastrointestinal absorption of calcium in granulomatous disease, vitamin D intoxication, lymphoma, and myeloma
      - actions on osteoclast bone resorption, GI absorption of calcium, and the urinary excretion of calcium.
      - Glucocorticoids are usually of no benefit in the treatment of primary hypercalcemia
  - Increase Urinary Calcium Excretion
    - Isotonic Saline +/- loop diuretic (lasix) when well hydrated
    - Goal is a daily urine output of 3 to 5 L
  - Diminish Bone Resorption
    - Calcitonin 4 IU/kg
      - Calcitonin resistance usually develops within 24 to 48 hours
    - Bisphosphonates
      - Drugs of choice for the treatment of life-threatening hypercalcemia
  - Dialysis
  - Chelation
    - EDTA or IV Phosphate
  - Mithramycin
    - inhibits the osteoclastic activity of parathormone - prompt lowering of serum calcium
    - The toxic effects (thrombocytopenia, hepatotoxicity, nephrotoxicity) limits its use
  - Calcium-lowering effects produced by NSAIDS in ectopic Hyperparathyroidism
- Surgical Management (Parathyroidectomy)
  - Treatment of primary hyperparathyroidism (and possible ectopic hyperparathyroidism)
  - General anesthesia is most commonly used for parathyroid surgery
  - Preop methylene blue or radioactive tracers may assist parathyroid tissue identification
  - Confirmation of successful resection may be made by observing a 50% decrease in the parathormone level, 5 min after removal, as compared with the preop level.
  - Normalization of serum calcium concentrations within 3 to 4 days and a decrease in the urinary excretion of cyclic adenosine monophosphate
- Secondary hyperparathyroidism
  - Seldom produces hypercalcemia
  - Treat underlying disorder

#### PRE-OPERATIVE MANAGEMENT / OPTIMIZATION

- Delay elective and non-urgent surgeries until calcium and other electrolyte levels are normalized
- Ensure adequate hydration and urine output prior to induction
- Preop methylene blue or radioactive tracers may assist parathyroid tissue identification
- Careful patient positioning – weak bones

#### ANESTHETIC OPTIONS

- No contraindications to any anesthetic technique
- General anesthesia is most commonly used for parathyroid surgery
  - Cervical Plexus block can be used

#### ANESTHETIC SETUP

- Standard CAS monitors
- Central venous pressure or pulmonary artery pressure monitoring
  - may be advisable in some patients requiring fluid resuscitation and diuresis
- Arterial Line for intra-operative PTH and Calcium measurement for parathyroid surgery

#### INTRA-OPERATIVE MANAGEMENT OF ANESTHESIA

- Careful patient positioning – risk of fractures

- Maintenance of hydration and urine output
- Mild hyperventilation may be beneficial however respiratory alkalosis also lowers serum potassium concentrations and leaves the actions of calcium unopposed
- Propofol can interfere with the PTH assay
  - many surgeons prefer that propofol not be used within 15 minutes of an assay

#### **POST – OPERATIVE MANAGEMENT**

- Monitor Calcium and Magnesium levels

#### **COMPLICATIONS**

- Post- Surgical
  - Recurrent Laryngeal Nerve Injury
    - Hoarseness if unilateral, Respiratory compromise if bilateral
  - Bleeding
  - Laryngospasm, Bronchospasm
  - Hypocalcemic tetany – worsened by hypomagnesemia
  - Acute arthritis
  - Hyperchloremic metabolic acidosis, in association with deterioration of renal function, may occur transiently
  - “Hungry bone” syndrome comes as a result of the rapid remineralization of bone - hypocalcemia

#### **REFERENCES**

- Co-existing, Toronto Notes, Barash, Miller, Chestnut, Anesthesiologist’s Manual of Surgical Procedures