Clinical aspects of endocrinology: parathyroid and adrenal gland disorders

Ahmad Moetamin

Kailash Bhatia

Abstract

The parathyroid glands are responsible for calcium homoeostasis, which is necessary for appropriate functioning of the musculoskeletal and nervous systems. Parathyroid adenoma remains the most common indication for surgery. Anaesthetic considerations for parathyroid surgery include good hydration, appropriate positioning, monitoring renal function along with serum electrolytes. The adrenal cortex is mainly responsible for secretion of mineralocorticoids, glucocorticoids, and androgens whereas the medulla consists of preganglionic sympathetic ganglion, which secretes epinephrine, norepinephrine and dopamine. Adrenocortical disease results in disturbance of water balance, electrolytes, cardiovascular instability and metabolic disturbances. Correction of water, electrolyte imbalance, blood pressure control with invasive monitoring, appropriate positioning, analgesia with appropriate hormone replacement therapy form the key principles of the anaesthetic management.

Keywords Anaesthesia; calcium; Cushing's syndrome; glucocorticoids; mineralocorticoids; parathyroid adenoma

Royal College of Anaesthetists CPD Matrix: 1A01, 2A03, 2A07, 3A07, 3100

Learning objectives

After reading this article you should be able to:

- outline the signs and symptoms of hypercalcaemia and hypocalcaemia encountered as a result of parathyroid dysfunction
- list the main hormones secreted by the adrenal gland
- describe the basic principles of anaesthetic management of patients presenting for parathyroid and adrenal surgery

Parathyroid gland

Surgical anatomy

Successful surgical management of parathyroid disease depends not only on correct biochemical diagnosis, but also on a good understanding of the anatomic locations of the parathyroid gland. About 84% of the patients have two superior and two inferior parathyroid glands. The superior parathyroid glands are located on the posterior-lateral aspect of superior thyroid lobe, usually outside the thyroid capsule. Inferior parathyroid glands lie near the lower pole of thyroid gland in the majority of patients.

About 13% of patients have supernumerary glands (found anywhere from thyroid to thymus) and about 3% of patients have only three glands.[1]

Ahmad Moetamin *MBBS FRCA DA is a Senior Specialist Trainee at Central Manchester University Hospital and St Mary's Hospital, Manchester, UK. Conflicts of interest: None.*

Kailash Bhatia *MBBS FRCA EDRA DA DNB is a Consultant Anaesthetist at Central Manchester University Hospital and St Mary's Hospital, Manchester, UK. Conflicts of interest: None.*

Supernumerary glands are responsible for persistent hyperparathyroidism after failed parathyroid surgery. Ectopic parathyroid glands (may be one of four or a supernumerary gland) can be found in the para-oesophageal space, in the mediastinum, intrathymic, intrathyroid, in the carotid sheath, or in a high cervical position.

Physiology

The parathyroid glands produce parathyroid hormone (PTH) that along with calcitriol (1,25-dihydroxyvitamin D) modulates calcium and phosphate homoeostasis.

PTH is responsible for rapid regulation of serum ionized calcium levels within a narrow range. Decrease in serum ionized calcium levels is sensed by calcium-sensing receptors (CaSR) present on the surface of parathyroid cells, which stimulate PTH secretion. PTH stimulates osteoclasts to release calcium and phosphate into the extracellular fluid, and increases phosphate excretion and calcium re-absorption by renal tubules. PTH also converts calcidiol (25-hydroxyvitamin D) to calcitriol (1,25-dihydroxyvitamin D) in renal tubular cells, which stimulate intestinal calcium absorption. Its coordinated actions on bone, kidney and intestine increase the flow of calcium into the extracellular fluid and increase the concentration of calcium in blood.[2] Increase in serum ionized calcium concentration inhibits the release of PTH. The normal PTH reference range is 10–65 ng/litre.

Parathyroid disease

Parathyroid disease can be classified into hyperparathyroidism and hypoparathyroidism.

Hyperparathyroidism is characterized by overproduction of PTH and hypercalcaemia.[3,4] It can be further classified as follows:

- **Primary hyperparathyroidism:** PTH secretion is inappropriately high in relation to serum calcium concentration. Up to 80–85% of cases of primary hyperparathyroidism are caused by a single adenoma, while 2–5% of cases are due to double adenomas. The UK incidence is estimated to be 25 per 100,000, and increases with age with the average age at diagnosis being 55 years. Multiple gland hyperplasia accounts for approximately 6% of cases of primary hyperparathyroidism. Parathyroid carcinomas account for 1–2% of cases of hyperparathyroidism.
  Some conditions are associated with primary hyperparathyroidism. For example, a family history must also be taken to identify familial hyperparathyroidism, multiple endocrine neoplasia (MEN) type I and MEN type II or

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familial hypercalcaemic hypocalciuria (FHH). Familial isolated hyperparathyroidism (FIHP) is a term given to familial primary hyperparathyroidism not associated with any other endocrine disorder.

- **Secondary hyperparathyroidism** is a condition in which PTH is elevated to compensate for chronically low concentration of calcium with no intrinsic parathyroid abnormality. Vitamin D deficiency and renal failure are the two most common causes of secondary hyperparathyroidism.
- **Tertiary hyperparathyroidism** is the condition in which parathyroid hyperplasia progresses to autonomous hypersecretion, so that excessive PTH secretion continues despite the presence of high concentration of calcium.
- **Ectopic or pseudohyperparathyroidism** is due to secretion of PTH by tissues other than the parathyroid gland. Carcinoma of the lung, breast, pancreas, oesophagus, or kidney are the most common.

Clinical presentation

The most common clinical presentation of hyperparathyroidism is asymptomatic hyperparathyroidism detected on biochemical screening.

The classic presentation of moans, groans, and stones is rarely seen in the developed world. The main manifestations of hyperparathyroidism and along with anaesthetic implications are highlighted in Table 1.

Medical management

For patients not undergoing surgery, following preventive measures are recommended:

- Avoiding factors that exacerbate hypercalcaemia like use of thiazide diuretics and lithium therapy, dehydration, prolonged bed rest, and a high calcium diet.
- Encouraging physical activity, which reduces bone resorption.
- Encouraging adequate hydration to reduce risk of renal stones.
- Decrease dietary intake.
- Maintain moderate vitamin D intake as decreased vitamin D stimulates PTH secretion.
- Cinacalcet (a calcimimetic) is used for patients with symptomatic and severe hypercalcaemia who are unable to have surgery and are on dialysis (NICE recommendation).[5] It normalizes serum calcium levels by activating the CaSR in the parathyroid gland and inhibiting PTH secretion.
- Bisphosphonates are recommended for patients with primary hyperparathyroidism and bone disease (osteoporosis or low bone mineral density) who wish to avoid surgery. It is a potent inhibitor of bone resorption.

Patients not undergoing surgery should have their serum calcium, renal function (creatinine, estimated glomerular filtration rate (eGFR)) and bone density monitored every 1–2 years.

Surgical management

The indications for surgery are as follows.

- Symptomatic primary hyperparathyroidism: parathyroid surgery is the only definitive therapy for symptomatic patients and it cures the disease, decreases the risk of kidney stones, improves bone mineral density and decreases fracture risk. Surgery also improves the functional quality of life and decreases the risk of death.[6]
- Asymptomatic patients:[7,8]

  For asymptomatic patients surgery is indicated if:
  - serum calcium concentration is 0.25 mmol/litre or more above the upper limit of normal
  - eGFR is <60 ml/minute
  - there is nephrolithiasis or nephrocalcinosis
  - 24-hour urinary calcium is >10 mmol/day
  - there is poor bone mineral density

Signs and symptoms of hypercalcaemia due to hyperparathyroidism

System	Manifestation	Consideration
Neuromuscular	Skeletal muscle weakness with hypotonia affecting proximal lower limb muscles	Reduced dose if muscle weakness. Monitoring of neuromuscular function. Resistance to muscle relaxants
Nervous system	Somnolence, psychosis, decrease pain sensation, cognitive changes, Decreased concentration, confusion	Appropriate preoperative assessment and documentation.
Renal	Polyuria, polydipsia, nephrolithiasis, renal failure, distal renal tubular acidosis, nephrogenic diabetes insipidus.	Fluid balance, good hydration, monitor renal function, ABG for acidosis, Rarely CVP monitoring. Dialysis in refractory hypercalcaemia
Cardiovascular	Hypertension, valvular calcification, arrhythmias, bradycardia, prolonged PR and short QT interval.	ECG, echocardiography in symptomatic patients, anti hypertensive therapy, arterial line if necessary.
Haematological	Anaemia	Monitor full blood count
Gastrointestinal	Abdominal pain, vomiting, peptic ulcer, pancreatitis.	Monitor LFT, amylase, consider PPIs in premedication, RSI if symptomatic.
Skeletal	Osteoporosis, osteitis fibrosis cystica, periarthritis, periarticular calcification, bone pain, pathological fractures.	Monitor calcium, phosphorus, and magnesium levels. Appropriate positioning during the perioperative period.

ABG, arterial blood gases; CVP, central venous pressure; ECG, electrocardiography; LFT, liver function test; PPI, proton pump inhibitor; RSI, rapid sequence Induction.

Table 1

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