**Prevention of hypocalcaemia after total thyroidectomy in children and adolescents**

**FULL DOCUMENT**

**Background**

Hypocalcaemia is the most common complication of total thyroidectomy and is secondary to insufficient parathyroid hormone (PTH) production. Hypocalcaemia due to primary hypoparathyroidism is generally transient, reflecting the mechanical trauma caused by total thyroidectomy on otherwise preserved parathyroid glands. In up to 4% of patients, it can be prolonged (>6-12 months) or permanent if the parathyroid glands have been removed or significantly damaged (1, 2).

Studies in adults reported incidences of hypocalcaemia ranging from 1 to 50%, with most centres around 20-30%. In contrast, paediatric studies found that 30 to 40% of children developed parathyroid dysfunction after total thyroidectomy, the majority transient (1, 4, 5). The nadir for hypocalcaemia usually occurs 24-48 hours postoperatively, although it may occur as early as 12 hours postoperatively or be delayed by 4 days (6).

Hypocalcaemia is associated with patient morbidity, mortality, increased length of stay and treatment costs. (7). Therefore, it is important to identify and monitor those at risk of post-thyroidectomy hypocalcaemia (PTHC) postoperatively so treatment and discharge be initiated in a timely manner.

**How to manage**

A pathway to streamline the perioperative assessment and management of patients undergoing total thyroidectomy is summarised in Figure 1.

1. **Preoperative management**

* Patient assessment should begin with ensuring normal serum 25-hydroxyvityamin D levels at least 1 month preoperatively.
* Give stoss dose cholecalciferol 150,000 IU if serum 25-hydroxyvitamin D is < 50 nmol/L if >12 months of age. If <12 months of age, refer to vitamin D guideline for treatment. (<https://www.rch.org.au/clinicalguide/guideline_index/Vitamin_D_deficiency/>)
* Surgical team to inform inpatient endocrinology team on the day of surgery.

Low preoperative serum 25-hydroxyitamin D level was also identified in some adult studies as a risk factor for PTHC (8-11).

1. **Intraoperative management**

Although a low intraoperative serum PTH level (<1.06-1.6 pmol/L) can also indicate higher risk of PTHC (4), this test is not readily available at RCH and therefore not routinely used. However, a postoperative PTH level may be helpful in guiding management of patients who do develop hypocalcaemia (see postoperative assessment below).

1. **Postoperative management**

Patients will be assessed and managed by the inpatient endocrinology team for hypocalcaemia

* Serum calcium (ionised calcium or total calcium and albumin) and PTH level should be performed within 6 hours postoperatively.

PTH testing with a timely turnover is not available at RCH and is therefore not likely to guide immediate treatment. However, once available, it can guide future management. A PTH of > 2.1 pmol/L in a normocalcaemic patient is reassuring (4). PTH of < 1.6 pmol/L is associated with higher risk of hypoparathyroidism and requires more intensive monitoring and slower wean of supplements (12). Clinical discretion should be used for PTH levels between 1.6 to 2.1 pmol/L in a normocalcaemic patient (4).

* Prophylactic calcium or calcium and calcitriol replacement should be started orally once patient is able to tolerate oral intake within 12 hours postoperatively.

Routine postoperative prophylactic replacement of calcium with or without calcitriol has been shown to reduce PTHC (13). Prophylactic calcium and calcitriol should be given to “high risk” patients (14, 15) and prophylactic calcium only to those with are “low risk”.

High risk patients

High risk patients are those who meets criteria for one of the following:

1. Parathyroidectomy
2. Parathyroid tissue damage or devascularisation/reimplantation
3. Lymph node or central dissection
4. Hyperthyroidism
5. Young age (≤ 6 years of age).

If the patient is a high-risk patient or develops biochemical hypocalcaemia (total calcium < 2.0 mmol/L or ionised calcium < 0.9 mmol/L), a starting dose of Calcitriol 0.025-0.05 mcg/kg/day should be commenced postoperatively as soon as possible *in addition* to oral calcium carbonate as detailed below (16).

Suggested prophylactic Calcitriol doses:

1. Age 1-5 years: Calcitriol 0.25 mcg BID
2. Age 6-10 years: Calcitriol 0.5 mcg BID
3. Age > 10 years and adults: Calcitriol 1 mcg BID

Please chart the same dose for PRN if patient develops symptoms of hypocalcaemia.

Note: In patients with hypocalcaemia, higher doses of up to Calcitriol 100 ng/kg/day (adult dose: 1 – 1.5 mcg daily) may be required if patient develops severe hypocalcaemia (16).

An as-required (i.e. PRN) calcium (dose guide in the low risk section below) and Calcitriol order as per the age/weight guidelines should also be charted for treatment of hypocalcaemia between scheduled doses (e.g. calcitriol 0.5 mcg PRN and elemental calcium 600 mg PRN if symptoms of hypocalcaemia, in a 7 year old, 25 kg child).

Calcium levels should be checked again at 12 hours postoperatively. If total serum calcium levels remain ≥ 2.0 mmol/L, then the patient can be discharged home once the surgical team has cleared the patient. If patient is discharged, serum calcium level should be rechecked 2-3 days after discharge.

Patients who develop hypocalcaemia

If the patient develops symptoms of hypocalcaemia (mild: muscle spasms or cramps, numbness or tingling periorally or in the extremities, fatigue; severe: tetany, seizures, laryngospasm, arrhythmia (prolonged QRS or QT), serum calcium and magnesium levels should be checked immediately. Treatment as per the “high risk” patients should commence as soon as possible. Calcium and calcitriol doses may be increased if patient develops hypocalcaemia while on calcium/calcitriol treatment. Intravenous calcium gluconate infusion should be considered only if the patient is unable to tolerate oral replacement, unless severe symptoms are present. As cutaneous necrosis and/or calcium deposition may occur with extravasation (17), care must be given to the intravenous site to ensure it is free flowing prior to and during administration. Rapid infusion can also cause bradycardia or cardiac arrest and therefore cardiac monitoring and/or PICU involvement is required (17).

Suggested IV calcium doses (3):

1. IV bolus: 10% calcium gluconate solution 0.5 mL/kg (0.11 mmol/kg of calcium ions), give diluted solution slowly over 20-60 minutes.
2. IV infusion: 10% calcium gluconate solution 4.5 mL/kg/day (1 mmol/kg/day of calcium ions), continuous infusion using an infusion pump.

(Note: Solution usually given diluted in a 1 to 5 fashion - Add 1 mL of Calcium Gluconate 10% to 4 mL of Glucose 5% or 10% to give a final volume of 5 mL = 0.044 mmol Calcium/mL. Consult: <https://www.rch.org.au/piper/neonatal_medication_guidelines/Calcium_Gluconate/> for more information. Also consider replacing magnesium if low.)

Discharge can be considered once symptoms of hypocalcaemia has resolved and total serum calcium levels are ≥ 2.0 mmol/L on 3 consecutive checks.

Low risk patients

All other patients who remains normocalcaemic and do not meet the “high risk” criteria above can be managed as “low risk” with prophylactic calcium replacement.

Suggested prophylactic oral calcium doses:

1. If weight < 30 kg, give elemental calcium 600 mg BID
2. If weight 30-49 kg, give elemental calcium 1200 mg BID
3. If weight > 50 kg, give elemental calcium 1200 mg TDS

Note: The starting treatment dose for hypocalcaemia is elemental calcium 50-150 mg/kg/day in 2-4 divided doses, up to an adult dose of elemental calcium 1.2g TDS orally. For example, Calcium carbonate 1.5 g (i.e. 1 Caltrate tablet) contains 600 mg of elemental calcium.

An as-required (i.e. PRN) calcium and Calcitriol order (dose as per the high risk guideline above) as per the age/weight guidelines should also be charted so that calcitriol is available on the ward should the patient develop symptoms of hypocalcaemia.

Calcium levels should be checked again at 12 hours postoperatively. If total serum calcium levels remain > 2.0 mmol/L, then the patient can be discharged home once the surgical team has cleared the patient.

**Follow up**

Full recovery from transient PTHC may take up to 6-12 months, and in up to 5% of the cases, hypoparathyroidism may be permanent.

For high risk patients

* Check serum calcium levels 2-3 days after discharge. If normal, check serum calcium levels weekly. If calcium remains within normal ranges, halve the Calcitriol or Calcium dose weekly until the patient is off both medications.

For low risk patients:

* Check serum calcium levels weekly. If calcium remains within normal ranges, halve the calcium dose weekly until they reach calcium carbonate 600 mg daily, then cease calcium if serum calcium level is normal 1 week after.

For patients who develop hypocalcaemia

* If the patient develops hypocalcaemia and/or requires calcium and/or calcitriol doses beyond the above suggested guides, ongoing discharge planning should be individualised as per the inpatient endocrinology team.

**Please note: all patients who undergoes total thyroidectomy should also start Thyroxine replacement postoperatively.**

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**Figure 1**. Pathway for the management of children following total thyroidectomy.



**Notes:**

1. PTH testing with a timely turnover is not available in many centres and is therefore not likely to guide immediate treatment. However, once available, it can guide future management. A PTH of > 2.1 pmol/L in a normocalcaemic patient is reassuring. PTH of < 1.6 pmol/L is associated with higher risk of hypoparathyroidism and requires more intensive monitoring and slower wean of supplements. Clinical discretion should be used for PTH levels between 1.6 to 2.1 pmol/L in a normocalcaemic patient.
2. High risk patients: Parathyroidectomy, parathyroid tissue damage or devascularisation/reimplantation, lymph node or central dissection, hyperthyroidism, young age (≤ 6 years of age).
3. Calcium dose is elemental calcium 50-150 mg/kg/day in 2 divided doses, up to an adult dose of elemental calcium 1.2g BID orally. As a guide:

If weight < 30 kg, give elemental calcium 600 mg BID

If weight > 30 kg, give elemental calcium 1200 mg BID

1. Calcitriol 0.025-0.05 mcg/kg/day should be started postoperatively for high risk patients or hypocalcaemic patients as soon as possible *in addition* to oral calcium carbonate as detailed above. As a guide:

Age 1-5 years: Calcitriol 0.25 mcg BID

Age 6-10 years: Calcitriol 0.5 mcg BID

Age > 10 years and adults: Calcitriol 1 mcg BID

If patient is hypocalcaemia and unable to tolerate oral treatment, IV calcium correction should be considered.

1. Symptoms of hypocalcaemia includes: muscle spasms or cramps, numbness or tingling periorally or in the extremities, fatigue, tetany, seizures, laryngospasm, arrhythmia (prolonged QRS or QT).

Ca Calcium

PTH Parathyroid hormone

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