Thyroid Supplements

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Uses

- More than 3 million chronic users in USA.
- T_4 prescribed for pts with chronic hypothyroidism.
- T_3 used in myxedema coma.
- T_3 successfully used as rescue therapy for cardiogenic shock after CPB.
- T_3 favorably administered to brain-dead donors before organ harvesting for heart or heart-lung transplantation. (Prophylactic use of T_3 has shown no benefit in recent randomized trials.)
- T_4 is generally administered PO; T_4 and T_3 can be administered IV.

Perioperative Risks

- Drugs (amiodarone, lithium, herbal supplements, catecholamines, radiopaque contrast media) and also cirrhosis, renal failure, sepsis, and operation (CPB) can induce euthyroid sick syndrome (reduced peripheral conversion of T_4 to T_3); may also precipitate myxedema coma.
- Amiodarone, a potent class III antiarrhythmic drug, is an iodine-rich compound with a structural resemblance to T_3 and T_4 and causes substantial iodine overload; with continued administration, may produce either thyrotoxicosis or hypothyroidism.

Worry About

- T_4 or T_3 can aggravate symptoms of myocardial ischemia.

Overview/Pharmacology

- Hypothyroidism (overt) estimated to affect 0.5–3.8% of adults and increases with age (over 15% of women at ≥age 60).
- After thyroidectomy, <30% of pts euthyroid at 10 y due to inadequacy or discontinuation of Rx.
- Reversal of clinical Sx of chronic hypothyroidism, including myocardial effusions, requires 2–4 mo Rx.
- Half-life of T_4 is 7 d; T_3 is 1.5 d.
- T_4 is a relatively inactive prohormone that undergoes monodeiodination in liver and kidney to biologically active T_3.

Drug Class/Mechanism of Action/ Usual Dose

- Thyroid hormone replacement Rx.
- T_3 binding to specific membrane receptor proteins augments membrane transport activity, mitochondrial oxidative phosphorylation, and protein synthesis.
- Extranuclear effects of T_3 occur within min, increasing myocardial mitochondrial and transmembrane transport activity.
- Nuclear effects of T_3 occur within 0.5–1 h, involving transcription and translation of myocardial enzymes and contractile proteins.
- Direct effect of T_3 decreases arterial smooth muscle tone.
- Usual dosage of T_4 is 0.15 mg/d PO.
- Acute Rx: T_4, 0.3–0.5 mg by slow IV infusion followed by 0.1–0.15 mg/d, or T_3, 0.005–0.01 mg IV.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Chronotropy, inotropy, reduced SVR Arrhythmogenesis	Less fatigue Palpitations	HR, reflexes	FT_4E, TSH, ECG
RESP	Restoration of hypoxic, hypercapnic ventilatory drive			
GI	Increased protein synthesis; enhanced hepatic, renal clearance/excretion functions		Normal skin turgor	
ENDO	Thermogenesis	Reversal of cold intolerance	Skin warm to touch	

Key Reference: Kohl BA, Schwartz S: Surgery in the patient with endocrine dysfunction, *Anesthesiol Clin* 27(4):687–703, 2009.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- Thyroid hormones increase breakdown of vitamin K–dependent clotting factors, which can alter coagulation status.
- Chronic amiodarone therapy may produce hyper- or hypothyroidism and has been specifically associated with thyrotoxicosis.
- Preop low free T_3 syndrome (FT_3 <2.23 pmol/L) has been associated with an increased risk of low cardiac output and death in coronary revascularization pts.

Induction/Maintenance

- T_4 administration is advocated in the management of organ donors; oral T_4 achieves approximately 91–93% of the bioavailability of IV thyroxine and also facilitates hemodynamic stability comparable with IV administration.
- Exaggerated Htn and tachycardia can occur with agents such as ketamine and exogenous catecholamines including ephedrine and epinephrine in pts on both acute and chronic thyroid hormone replacement.

Adjuvants/Regional Anesthesia/Reversal

- Anticholinergics with minimal CV effects (e.g., glycopyrrolate) preferred over atropine.
- Caution in the presence of spinal anesthesia; T_3 administration may produce aggravated hypotension.

Postoperative Period

- Cirrhosis, sepsis, renal failure, surgery may all decrease peripheral conversion of T_4 to T_3 (euthyroid sick syndrome) and precipitate hypothyroidism.

Anticipated Problems/Concerns

- In critically ill pts, T_3 replacement can produce detrimental increases in oxygen requirements (especially myocardial) and protein catabolism without improving mortality rates.

Tissue Plasminogen Activator

Alan David Kaye | Burton D. Beakley | Ken F. Mancuso

Uses

- Clinical indications for thrombolysis in treatment of pulmonary embolism, acute ischemic stroke, acute MI, and occluded central venous access devices.
  - MI: Administration as soon as possible from symptom onset
  - Stroke: Administration within 3 h from onset of symptoms
- Rapid clot lysis by t-PA offers advantages in comparison with streptokinase.
- May be used in combination with other anticoagulants such as heparin and aspirin. Also may be combined with beta-blockers, morphine, nitroglycerin, and plt IIb/IIIa blockers.

Perioperative Risks

- Increased risk of bleeding during surgery; if severe, possible need for blood transfusion, fresh frozen plasma, cryoprecipitate, and plt infusion therapy.
- Strict blood pressure monitoring with intraop Htn posing increased risk of intracranial hemorrhage (0.8% with acute MI therapy and 6% with acute ischemic stroke therapy).
- Incomplete restoration of coronary blood flow and persisting thrombogenicity may lead to cardiac instability and risk for periop infarction.

Worry About

- Severe hemorrhagic complications and intracranial hemorrhage.
- Invasive procedures: Damage to blood vessels during vascular access procedures can cause severe bleeding, especially at noncompressible sites (e.g., subclavian vein).
- Risk for hematoma formation causing damage via mass effect to surrounding tissue/vessels (e.g., ulnar nerve during arterial cannulation).
- Contraindication for spinal/regional anesthesia.
- Bleeding at venipuncture sites.

Overview/Pharmacology

- Thrombolytic agent: Natural t-PA is produced by vascular endothelial cells and is naturally released from the endothelium in response to venous occlusion, physical activity, stress, or vasoactive medications. Responsible for most of the body's effort to prevent excessive thrombosis.
- Accelerates the conversion of plasminogen (bound to fibrin) to plasmin, resulting in fibrinolysis as site of clot.
- Time-dependent, because older thrombi develop extensive fibrin polymerization, making them more resistant to thrombolysis.
- t-PA (alteplase) is commercially produced using cDNA for natural t-PA, which is then is transfected into a mammalian cell line.
- Initial thrombolytic response is seen within 30 min when given IV. Half-life is about 5 min; elimination half-time is about 30–50 min. Some 80% is cleared from plasma within 10 min of stopping a standard infusion, and clearance is via the liver.