Goals
1. Understand the physiological and biological changes associated with hyperthyroidism and thyrotoxicosis.
2. Discuss the management of anesthesia in a patient with hyperthyroidism.
3. Evaluate the postoperative complications of thyroidectomy.
4. Discuss the perioperative diagnosis and management of a thyroid storm.

Case
Patient is a teenager who underwent total thyroidectomy secondary to medical treatment failure. Patient had hyperthyroidism but was non-compliant to medical treatment and to clinical or laboratory follow-up visits. Patient had undergone an uneventful surgery, was extubated and transferred in a stable condition. Five hours postoperatively, vital signs were tachycardia at 145 bpm, hypertension at 160-170/100 mm Hg and a respiratory rate of 45/min. Pain control had been adequately achieved with intravenous morphine. Elevated blood pressure and heart rate were treated with intermittent intravenous propranolol. Few hours later, patient complained of dyspnea and dysphagia. You are the anesthesiologist on-call that night, and requested to the bedside of a patient for an urgent tracheal intubation.

Questions
1. What are the signs, symptoms and causes of hyperthyroidism? How would you evaluate a patient with hyperthyroidism preoperatively?
2. How would you manage this patient intraoperatively?
3. What are the possible complications after a surgical procedure involving the thyroid gland? This patient was found to have an enlarging hematoma in her neck. How would you manage this complication?
4. What are the precipitating factors of occurrence of a thyroid storm?
5. A thyroid storm post total thyroidectomy. Is it possible?
Discussion

The hypothalamus releases thyrotropin-releasing hormone (TRH), which traverses the pituitary stalk and stimulates release of thyroid-stimulating hormone (TSH) from the anterior pituitary. TSH is released in to the circulation and controls production and release of $T_4$ and $T_3$. Some $T_3$ is secreted by the thyroid, but most is produced by deiodination of $T_4$ in peripheral tissues. Both $T_4$ and $T_3$ are bound to carrier proteins (principally thyroid-binding globulin, TBG) in the circulation.

Different steps are involved in thyroid hormone synthesis:
1): Uptake of iodide. Iodide from the bloodstream is concentrated in thyroid cells by an active transport mechanism.
2): Iodination of thyroglobulin. Thyroglobulin, a large glycoprotein rich in tyrosine, is enzymatically iodinated and stored in the thyroid follicles.
3): Coupling reactions: The mono-iodotyrosine and diiodothyrosine moieties within the thyroglobulin molecule are coupled to one another to form triiodothyronine ($T_3$) and thyroxine ($T_4$).
4): Release of hormones. $T_3$ and $T_4$ are enzymatically cleaved from thyroglobulin within the follicular cell and released into the bloodstream. $T_3$ and $T_4$ inhibit release of TSH and to a much smaller degree the release of TRH, thus establishing a negative feedback control mechanism.

The thyroid secretes thyroxine ($T_4$) and triiodothyronine ($T_3$), which influence basal metabolic rate, cardiac and neurological function. Diseases of the thyroid may be manifest by quantitative or qualitative alterations in hormone secretion, enlargement of the gland, or both. Under or overproduction of thyroid hormones is usually reflected in decrease or increase of serum $T_4$ and $T_3$ levels. When TBG is elevated or low, the free thyroxin index (FTI) corrects serum $T_4$ for alterations in binding protein and thus provides an index of thyroid status.

Different varieties of thyrotoxicosis:
- Disorders associated with thyroid hyperfunction: due to excess production of TSH (rare) or an abnormal thyroid stimulator such as Graves’ disease/ trophoblastic tumor or intrinsic thyroid autonomy such as a hyperfunctioning adenoma/toxic multinodular goiter.
- Disorders not associated with thyroid hyperfunction: due to disorders of hormone storage such as subacute thyroiditis/chronic thyroiditis with transient thyrotoxicosis or an extrathyroid source of hormone such as thyrotoxicosis factitia/ ectopic thyroid tissue (Stroma ovarii, Functioning follicular carcinoma).

Hyperthyroidism in children is most commonly congenital or a result of Graves’ disease. Congenital hyperthyroidism is caused by the transfer of maternal thyroid-stimulating immunoglobulins in utero. These infants may be premature, and tachycardia, respiratory distress, and congestive heart failure may be present along with physical appearance of
goiter. Conversely, Graves’ disease occurs more frequently among adolescents than children and 4 to 5 times more frequently among females.

Many symptoms and signs are associated with hyperthyroidism. They are the same for all hyperthyroidism with some exceptions, such as infiltrative ophtalmopathy and dermopathy, which are confined to Graves’ disease. The clinical presentation may be dramatic or subtle.

The more common signs are: (1) goiter; (2) tachycardia; (3) widened pulse pressure; (4) warm, fine, moist skin; fingernails may separate from the nail bed (5) tremor (97%); (6) eye signs (71%) and (7) atrial fibrillation (10%). In hyperthyroidism, the metabolic rate of the body is increased, causing significant changes in the cardiovascular system, proportional to the severity of the thyroid dysfunction.

The most frequent symptoms are: (1) nervousness and increased activity (99%), (2) increased sweating, (3) hypersensitivity to heat, (4) palpitations, (5) fatigue, (6) increased appetite, (7) weight loss, (8) tachycardia, (9) insomnia, (10) weakness, and (11) frequent bowel movements. Eye signs noted in patients with thyrotoxicosis include stare, lid lag, lid retraction, and mild degrees of conjunctival injection or edema-producing symptoms including orbital pain, lacrimation, irritation, and photophobia. Infiltrative ophtalmopathy is a more serious development and is specific for Graves’ disease. It is characterized by increased retro-orbital tissue, producing exophthalmos, and by lymphocytic infiltration of the extraocular muscles, producing a spectrum of ocular muscle weakness frequently leading to blurred and double vision. The pathogenesis of infiltrative ophtalmopathy is poorly understood. It may occur before the onset of hyperthyroidism or as late as 15 to 20 yr afterwards and frequently worsens or improves independent of the clinical course of hyperthyroidism.

Infiltrative dermopathy, also known as pretibial myxedema (a confusing term, since myxedema suggests hypothyroidism), is characterized by nonpitting infiltration of mucocinous ground substance, usually in the pretibial area. The lesion is very pruritic and erythematous in its early stages and subsequently becomes brawny. Like ophtalmopathy, infiltrative dermopathy may appear years before or after hyperthyroidism.

The diagnosis of hyperthyroidism is usually straightforward and depends on a careful clinical history and physical examination, a high index of suspicion, and routine thyroid hormone determinations. A serum T4 assay and a T3 resin uptake test are a highly accurate combination of initial tests for assessing thyroid status. Mild to moderate hyperthyroidism may be difficult to diagnose clinically during pregnancy since many normal parturients experience tachycardia, heat intolerance, and emotional instability. In hyperthyroidism: There is increase in T4, increased RT3U, increased T3, while in pregnancy there is increased T4, decreased RT3U, and normal T3. Age-adjusted normal values are needed because thyroid hormone levels are higher in children.

Preoperatively, elective surgery should be deferred until the patient has been rendered euthyroid and the hyperdynamic cardiovascular system has been controlled with a beta antagonist, as evidenced by an acceptable resting heart rate. The child should have
received ablation treatment to ensure a euthyroid state confirmed by preoperative thyroid function tests. All drugs being administered to manage the hyperthyroid state should be continued through the perioperative period. One week before surgery, administration of Lugol’s iodine solution should be initiated to decrease vascularity and hyperplasia of the overreactive gland.

When surgery cannot be delayed in a symptomatic hyperthyroid patient, the continuous infusion of a beta-blocker may be useful for the control of cardiovascular responses evoked by sympathetic nervous system stimulation. Poor control of hyperthyroidism and surgery are associated with an increased risk of the development of thyroid storm. Anxiety relief is often provided by the oral administration of a benzodiazepine. The use of an anticholinergic drug is not recommended, since such a drug could interfere with the body’s normal heat-regulating mechanism and contribute to an increase in heart rate. Evaluation of the upper airway for evidence of obstruction is an important part of the preoperative preparation. A large goiter requires a computed axial tomography scan to determine if tracheal compression or deviation exists. Propranolol may be used preoperatively to control tachycardia.

Induction of anesthesia is acceptably achieved with a number of intravenous induction drugs. Thiopental has been an attractive selection because its thiourea structure lends antithyroid activity to the drug. Nevertheless, it is unlikely that a significant antithyroid effect will be produced by an induction dose of this drug. Ketamine is not an appropriate selection because it can stimulate the sympathetic nervous system. Indeed, tachycardia and hypertension have been described after administration of ketamine to euthyroid patients being treated with thyroid hormone replacement. Propofol clearance and distribution volume increase in patients with hyperthyroidism Assuming the absence of airway obstruction from an enlarged goiter, the administration of succinylcholine or of a nondepolarizing muscle relaxant that will not affect the cardiovascular system is useful to facilitate intubation of the trachea.

Constant monitoring of body temperature is particularly useful; methods to lower body temperature, including a cooling mattress and cold crystalloid solutions for intravenous infusion are recommended. The patient with exophtalmos is susceptible to corneal ulceration and drying, emphasizing the need to protect the eyes during the perioperative period.

The selection of a muscle relaxant should include consideration of the potential impact of this drug on the sympathetic nervous system. Pancuronium is not an appropriate selection, in view of the ability of this drug to increase heart rate and thereby mimic sympathetic nervous system stimulation.

Goals during maintenance of anesthesia for a hyperthyroid patient are to avoid the administration of drugs that stimulate the sympathetic nervous system and to provide sufficient anesthetic depression to prevent an exaggerated response to surgical stimulation. The possibility of organ toxicity owing to altered or accelerated drug metabolism in the presence of hyperthyroidism must also be considered when selecting drugs for maintenance of anesthesia. The use of volatile agents is acceptable. Increased cardiac output and temperature may result in an increased minimum alveolar concentration (MAC) for the volatile agents. High dose narcotics would be required to
provide adequate inhibition of the sympathetic nervous system. Muscle relaxation with non depolarizing agents with minimal cardiac effects is preferable. A prolonged response to nondepolarizing agents may occur in patients with preexisting muscle weakness. Hypercarbia will result in stimulation of the sympathetic nervous system and should therefore be avoided. In the presence of tachycardia, the use of beta-blockade during the perioperative period is essential. Treatment of hypotension, if needed, is best achieved with the use of a direct-acting agent such as phenylephrine, rather than agents such as ephedrine, which act in part by an indirect mechanism. Constant monitoring of body temperature is essential.

Regional anesthesia with its associated blockade of the sympathetic nervous system is a potentially useful selection for the hyperthyroid patient, assuming there is no evidence of high-output congestive heart failure. Epinephrine is to be avoided in the local anesthetic solution, as systemic absorption of this catecholamine could produce an exaggerated circulatory response.

**Thyroid storm** is an acute exacerbation of hyperthyroidism. It is caused by the sudden excessive release of thyroid gland hormones into the circulation. Thyroid storm, which is rare in children, results from untreated or inadequately treated thyrotoxicosis and may be precipitated by infection, trauma, surgery, embolism, diabetic acidosis, fright, toxemia of pregnancy or labor, discontinuance of antithyroid medication, or radiation thyroiditis. Thyroid storm is a life-threatening emergency requiring prompt and specific treatment. It may mimic malignant hyperthermia, but often lack muscle rigidity, severe acidosis and myoglobinuria.

**Treatment of a thyroid storm** must be immediate and should occur in an acute / intensive care setting. Blood measurements including thyroid function levels should be withdrawn. Treatment should consist of an infusion of cooled crystalloid solutions and continuous infusion of a beta blocker (esmolol), to maintain the heart rate at an acceptable level. When hypotension is persistent, the administration of cortisol should be considered. Dexamethasone may inhibit the conversion of T₄ to T₃, an effect that is additive to propylthiouracil. Aspirin may displace T₄ from its carrier protein and is not recommended for lowering body temperature. It is also important to treat any suspected infection. Ultimately, antithyroid drugs such as propylthiouracil and sodium iodide should be added. Definitive therapy after control of the crisis consists of ablation of the thyroid gland with ¹³¹I or surgery.

**Summary:** This non compliant patient showed clinical signs of thyroid storm even after complete removal of the thyroid gland. In the adolescent and young adult, the fractional rate of turnover of T₄ in the periphery is normally about 10%/d (half-life, 6.7 d). The half-life of thyroxine is inversely related to the initial serum thyroxine levels. Large quantities of thyroglobulin are released into the blood during surgical manipulation of the thyroid. Metabolic and hemodynamic manifestations of thyrotoxicosis may be masked intraoperatively by anesthetics and sedation and exaggerated in the postoperative period. The diagnosis of a thyrotoxic crisis is made entirely on the clinical findings. Most importantly, there is no difference in thyroid hormone levels between patients with "uncomplicated" thyrotoxicosis and those undergoing a thyroid storm. Any delay in
therapy, e.g. by awaiting additional laboratory results, must be strictly avoided, because the mortality rate may rise to 75%.

References:


