North Asian International Research Journal of Multidisciplinary

CIF IMPACT FACTOR:4.465

ISSN: 2454-2326 Vol. 4, Issue-1 January-2018

Index Copernicus Value 58.12 Indexed As Per MCI

INVESTIGATION OF THYROID EMERGENCIES

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INTRODUCTION

Thyroid crises contain a miniscule portion of patients with thyroid brokenness, who arrive up hospitalized in the emergency unit as a result of their strange thyroid physiology or life structures. As these conditions are rarely experienced in the ICU, a legitimate comprehension of the hormonal pathophysiology and differed clinical highlights will prompt suitable and convenient foundation of hormonal and strong treatment, at last rendering survival advantage to the patient. The accompanying conditions constitute thyroid crises: I) thyroid tempest, ii) hypothyroid trance like state, and iii) monstrous goiter causing pressure of the aviation routes and expansive veins.

THYROID STORM

It is also known as thyroid crisis or thyrotoxic crisis and is an extreme physiological condition due to thyroid hormone excess. A very severe, life threatening and decompensated form of thyrotoxicosis, it is rare (seen in 1-2% of patients admitted for thyrotoxicosis); but mortality rates approach 10-20%. Thyroid storm may be seen even in patients who have not been diagnosed with hyperthyroidism. The male to female ratio is 1:3.

Causes: i) Grave's disease, ìi) Toxic multinodular goiter, iii) Solitary nodular goitre iv) Subacute thyroiditis v) Postpartum thyroiditis, vi) Thyrotoxicosis factitia, vii) Metastatic thyroid malignancy.

Whatever the etiology of hyperthyroidism, its conversion to thyroid storm requires the addition of precipitating factors.

Precipitating factors: i) Infection, ii) Trauma, iii) Surgery- of the thyroid gland or non-thyroidal, iv)Acute myocardial infarction or Acute coronary syndrome, v) Pregnancy, labor, complicated delivery vi) Burns vii) Medical illnesses- congestive heart failure, diabetic ketoacidosis, cerebrovascular accident, pulmonary thromboembolism, sepsis, viii) Stress- emotional ix) Abrupt interruption of thyroid drug therapy, x) Administration of iodine compounds or radioiodine (I^{131} or I^{123}), xi) Others- chemotherapy for leukemia, radiation therapy to neck malignancies, aspirin overdose, organophosphate poisoning, exercise, status epilepticus and drugs (tyrosine kinase inhibitors, lithium, biological agents like interleukin 2 and interferon).

Clinical features: i) Central Nervous System- apathy, agitation, delirium, confusion, paranoia, and coma. ii) Cardiovascular System- congestive heart failure, tachyarrhythmia (atrial fibrillation, supraventricular tachycardia, ventricular tachycardia and ventricular fibrillation,) sinus tachycardia, dilated cardiomyopathy, high cardiac

output state, and pulmonary hypertension. iii) Gastrointestinal tract- vomiting, diarrhoea, jaundice, diffuse abdominal pain occasionally presenting as acute abdomen. iv) Respiratory system- dyspnea, tachypnea and acute respiratory failure. v) Thermoregulation- fever, hyperthermia and diaphoresis. vi) Nutrition- weight loss. vii) Renal- proteinuria, acute renal failure.viii) Electrolyte disturbances- hypercalcemia, ketoacidosis, lactic acidosis. viii) Hematology- leucocytosis, hypercoagulable state leading to thromboembolism.

Some elderly patients may have very few signs of hyperthyroidism and present with stupor, apathy, coma, and congestive heart failure (apathetic thyroid storm).

Diagnosis: i) It usually needs to be based on clinical judgment and treatment started even before laboratory results are available. A semiquantative scale developed by Burch and Wartofsky can be used to definitively identify patients with thyroid storm. ii) Thyroid function tests(TFT): TFTs reveal increase in free T3 and free T4 while TSH will be very low (even undetectable). iii) Other laboratory investigations: Serum bilirubin, transaminases, blood glucose levels may be increased while potassium and total cholesterol may be decreased.

OBJECTIVES

- Enumerate thyroid diseases which will land the patient in the intensive care unit;
- Describe the clinical features, investigation and treatment of throid storm;
- Describe the clinical features, investigation and treatment of hypothyroid coma; and
- Describe the clinical features, investigation and treatment of obstructive symptoms due to goiter.

Treatment

Principles of treatment: i) Treat the hyperthyroid state. ii) Prevent the effects of circulating T3 and T4. iii) Treat the multiorgan dysfunction. iv) Treat the precipitating cause.

i) Treat the hyperthyroid state:

1) Prevent new thyroid hormone synthesis (Thionamides) 2) Prevent new thyroid hormone release (Thionamides) 3) Prevent conversion of circulating T4 to T3 (steroids, lithium, high dose iodine and iodinated contrast medium)

Thionamides: Propylthiouracil, Carbimazole, Methimazole are used in the treatment of hyperthyroid state.

Propylthiouracil (PTU): a) Dose: Loading dose- 500-1000 mg followed by a maintenance dose of 250 mg every 4-6 hours. b) It additionally prevents peripheral conversion of T4 to T3. c) It is given either orally (if patient is conscious and able to swallow) or through the nasogastric tube or rectally. d) Onset of action is rapid. e) PTU has potential for hepatotoxicity. f) Hence it is preferred now only in pregnancy, where other thionamides cannot be used.

Methimazole or Carbimazole: a) Dose: 20-30 mg every 4-6 hours may even go up to 60-80 mg every 4-6 hours. b) They are preferred over PTU unless the patient is pregnant. c) They can be given orally, through the nasogastric tube, rectally, or even intravenously.

Steroids: a) Hydrocortisone is used in the dose of 100 mg intravenously or intramuscularly every 6 hours and continued till the condition of the patient improves completely. b) If Dexamethasone is used, the dose is 2 mg intravenously every 6 hours. c) Doses of both the drugs need to be tapered appropriately before they are stopped.

Lithium: a) Dose: 1200 mg per day in 3-4 divided doses. b) Lithium is used if thionamides are contraindicated and patient is allergic to iodine. c) Serum lithium levels are monitored to prevent toxicity.

High dose Iodine: a) Lugol's iodine or potassium iodide solution is used. b) Dose: 0.3 ml or 10 drops of Lugol's iodine diluted to 50 ml every 8 hours, orally or through the nasogastric tube. c) Its action is due to the Wolff-Chaikoff effect leading to the suppression of thyroid hormone release and peripheral conversion of T4 to T3. d) It should be administered at least one hour after administration of thionamide drugs. e) Sodium iodide may be used intravenously (dose- 500-1000 mg), but it is not easily available as a sterile solution.

Iodinated contrast solution: 0.5-1 gm every 12 hours.

Cholestyramine at a dose of 4gm, 2-4 times a day orally, reduces enterohepatic circulation of thyroid hormones. In refractory cases, plasma exchange, peritoneal dialysis or hemofiltration may be used to reduce the circulating thyroid hormones.

ii) Prevent the effects of circulating T3 and T4:

Beta blockers: 1) They block the hyperadrenergic effects of the excessive thyroid hormones. 2) They can be used if there are no contraindications to their use (history of asthma, COPD or congestive heart failure). 3) They must be used with continous cardiac monitoring. 4) Propranolol is used most commonly at the dose of 60-80 mg, three times a day, orally or through the nasogastric tube. It may also be used intravenously at the dose of 10 mg; at the rate of 0.5-1 mg per minute till heart rate is less than 100 per minute and then continued orally as above. 5) If propranol is contraindicated, cardioselective betablockers (metoprolol, atenolol), calcium channel blockers or digoxin may be used. 6) Esmolol, an ultra short acting beta blocker, is preferred by some, as an intravenous infusion of 50-100 mcg/kg/min with a loading dose of 250-500 mcg/kg.

iii) Treat the multiorgan dysfunction:

1) Manage the patient in intensive care unit. 2) Take care of ABC (airway, breathing, and circulation). 3) Respiratory support with oxygen therapy or mechanical ventilation (noninvasive or invasive) as required. 4) Resuscitation and hemodynamic support- Intravenous infusions to correct fluid and electrolyte disturbances. 5) Antipyretics- cooling mattresses and cold sponging are used along with paracetamol to reduce the raised temperature. Salicylates are avoided as they reduce thyroid hormone binding to thyroglobulin and may in fact worsen thyroid storm. 6) Treat hypertension. 7) Treat delirium and agitation by sedation with haloperidol and benzodiazepines. 8) Provide nutritional support with adequate dextrose infusions and vitamin (especially thiamine) supplementation. 9) Treat the tachyarrythmias with antiarrythmic drugs if patient is hemo- dynamically stable or by electrical cardioversion if unstable. Treat congestive heart failure with diuretics and ACE inhibitors.

iv) Treat the precipitating cause:

1) Search and treat the focus of infection. 2) Use broad spectrum antibiotics on empiric basis as appropriate. 3) Send urine and blood cultures. 4) Treat trauma, diabetic ketoacidosis, myocardial infarction and other precipitating factors as per usual principles.

Once thyroid storm has been treated the hyperthyroid state should be treated definitively with antithyroid drugs, radioiodine or thyroidectomy.

HYPOTHYROID COMA

It is also known as myxedema coma or myxedematous coma and is due to very severe, untreated hypothyroidism manifesting with reduced temperature and altered mental status. It is an emergency to be treated in an ICU and has high mortality, but fortunately it is rare. Typically the patient is an elderly female with history of hypothyroidism with or without adequate treatment, who may have stopped treatment, or may have suffered an intercurrent stressful situation (infection). Occasionally coma may be the first presentation of hypothyroidism. Rarely hypothyroid coma may be seen in young females, some of whom may be pregnant.

Precipitating factors: i) Burns, ii) Trauma, iii) Surgery, iv) Severe infection- pulmonary or urinary tract infection, sepsis, v) Low ambient temperature, vi) Cardiac diseases- myocardial infarction, congestive heart failure, vii) Cerebrovascular accident viii) Labour, ix) Anesthesia x) Drugs- neuroleptics, sedatives (benzodiazepines), xi) Intake of large amounts of liquids, xii) Seizures, xiii) Gastrointestinal bleeding.

Some of the common causes of hypothyroidism are: i) Chronic autoimmune thyroiditis, ii) Thyroidectomy (total or partial), iii) Graves disease treated with radioiodine, iv) Secondary hypothyroidism- hypopituitarism, v) Drugs- amiodarone, lithium.

Clinical features: i) Hypothermia- is usually severe with temperature approximately 26.7^0C (80^0F). Rarely, temperature may even reach 21^0C. In some cases, temperature may be normal in the presence of infection. ii) Altered mental status- may present as disorientation, depression, paranoia, hallucination, cerebellar signs, amnesia, disturbed memory, abnormal EEG findings, seizures, status epilepticus, stupor, obtundation or coma. iii) Cardiovascular system- abnormalities present as bradycardia, prolonged QT interval, varying degrees of AV block, ventricular arrhythmias (torsades de pointes), pericardial effusion, reduced cardiac output or shock. iv) Respiratory system- disturbances present as hypoventilation and hypercarbia or respiratory failure requiring mechanical ventilation. v) Renal and electrolyte disturbances- manifests as hyponatremia, edema, retention of urine or rarely renal failure. vi) Gastrointestinal- manifestations are constipation, paralytic ileus, ascites, gastroparesis, and gastrointestinal bleeding. vii) Hematological- problems are coagulopathy due to vonWillebrand syndrome and reduction of coagulation factors, DIC (disseminated intravascular coagulation), granulocytopenia and microcytic or macrocytic anemia. viii) General- manifestations of hypothyroidism like macroglossia, ptosis, generalized skin swelling or cool dry skin, periorbital edema, obesity and depressed deep tendon reflexes.

Diagnosis: i) It should be suspected clinically. ii) TSH is raised in most cases. It may rarely be normal in pituitary causes of hypothyroidism. Severe systemic illness and drugs (inotropes, steroids) used to treat the associated systemic illness will cause blunting of the TSH elevation. iii) T3 and T4 levels are low. iv) Hyponatremia, hypoglycemia, hypoxia, respiratory acidosis, hypercapnia, hypercholesterolemia and elevated LDH and serum creatinine kinase levels may be present.

Treatment

Principles of treatment: i) Thyroid hormone supplementation. ii) Steroids. iii) Correction of fluid and electrolyte disturbances. iv) Treatment of precipitating cause.

i) Thyroid hormone supplementation: a) Supplementation with L-thyroxine with or without addition of liothyronine. b) Therapy is preferably intravenous. c) There is no consensus on the best therapeutic regime. d) Dose of L-thyroxine- High dose (300-400mcg on day 1 and then 50-100 mcg/day on subsequent days) is

preferred by some. Though tolerated by young patients, it may cause sudden cardiac death in the elderly. Hence a lower dose is preferred (100mcg on day 1 and then 50-100mcg on subsequent days). e) Liothyronine- at a dose of 10-25 mcg (bolus), intravenously and then 10 mcg intravenously every 4 hours for the first 24 hours and every 6 hours over the next 48 hours and then oral therapy with L-thyroxine (50-100 mcg daily), as feasible. Initial therapy with liothyronine may be preferred, as it has better bioavailability and peripheral conversion of T4 to T3 is impaired in hypothyroid coma. Care should be taken during liothyronine therapy as excess T3 may increase mortality. f) Combined T4+T3 approach: to avoid above complications, a combined approach with L-thyroxine and liothyronine is advised as shown in Table no. 1.

Table No. 1 Combined L-thyroxine and liothyronine therapy

Dose	L-thyroxine	Liothyronine
Initial	250 mcg i.v./orally/NGT	10 mcg i.v.
Over 24 hours		10 mcg i.v., 8-12 hourly
After 24 hours	100 mcg i.v./orally/NGT	Continue above dose
After 48 hours	50-100 mcg i.v./orally/NGT	Continue above dose
After 72 hours	Maintenance therapy with L-throxine (50-100 mcg orally/ NGT)	

ii) Steroids: a) Hydrocortisone at a dose of 50-100 mg intravenously every 6 hours, is preferred. b) It is required to treat the associated adrenal insufficiency.

iii) Correction of associated fluid, electrolyte and other disturbances: a) Maintain airway and provide mechanical ventilation if necessary. b) Hyponatremia- is a frequent occurrence and needs correction by restricting water intake or by intravenous infusion of isotonic saline (if serum sodium is less than 120). If hyponatremia is more severe, infusion of 3% NS is used very carefully. Occasionally, Conivaptan may be used in patients with euvolemic or hypervolemic hyponatremia. c) Hypothermia- is treated with passive and gradual heating with blankets and air warmers.

iv) Treatment of precipitating cause: a) Appropriate antibiotics (broad- spectrum) are started for bacterial infections. b) Diuretics are used to treat volume overload and pulmonary edema. c) Intravenous glucose is used in the presence of hypoglycemia d) Inotropes are used if shock is present while digoxin is used with care for congestive heart failure.

AIRWAY AND VASCULAR OBSTRUCTION DUE TO GOITRE

Gross enlargement of the thyroid gland, especially substernal and intrathoracic extension, causes compression of the airway and the great vessels at the thoracic inlet. Sometimes massive hemorrhage inside a thyroid nodule, malignant thyroid disease, metastasis to thyroid gland and Reiter's thyroiditis may cause compressive symptoms.

Symptoms and signs: i) Dyspnea- usually chronic with acute or subacute exacerbations, ii) Stridor, dysphonia, iii) Dysphagia, choking, iv) Fullness and pressure in neck, v) Superior vena cava syndrome- causing facial edema, cyanosis and venous engorgement of face and arms, vi) Esophageal varices, vii) Phrenic or laryngeal nerve paralysis, viii) Horner's syndrome, ix) Chylothorax, and x) Sleep apnea.

Treatment: a) Continous positive airway pressure (CPAP) application or intubation and mechanical ventilation for maintaining patency of the airways and to treat respiratory distress. b) In a few cases where intubation is not possible, emergency tracheostomy may be required. c) Surgery to relieve the obstruction in the form of thyroidectomy and associated sternotomy, if required. d) Radioiodine and percutaneous laser ablation may be preferred in some patients.

CONCLUSION

Thyroid storm occurs in hyperthyroid patients in the presence of precipitating circumstances leading to a hyperadrenergic condition which is fatal unless treated with care. It is treated with thionamides, beta blockers and correction of abnormal organ function. Hypothyroid coma usually presents in the winter months, in elderly females, in the presence of a precipitating cause. The patient has profound hypothermia and altered mental status or coma. It is treated with supplementation of thyroid hormones and treatment of the associated multiorgan dysfunction. Obstruction of the airway and blood vessels in the neck by an enlarged thyroid gland is very rare.

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