Thyroid Emergencies: New Insight into Old Problems

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Abstract

Thyroid emergencies are major life-threatening endocrine conditions associated with life-threatening disorders resulting from either severe deficiency or excess of thyroid hormones. Deficiency of thyroid hormones may present as myxedema coma whereas excessive hormone production can present as life threatening thyrotoxic storm. The diagnosis of both requires a high index of clinical suspicion. Thyroid storm, in spite of accurate diagnosis, continues to have high fatality, whereas myxedema management has markedly improved with advancement in intensive care facility. The key to successful management of these emergencies is timely diagnosis and management by experienced physician in an intensive care setting. This article discusses the basic differences of both entities with an attempt to appropriate recognition and awareness of clinical signs and symptoms, highlight the salient diagnostic points and delineate the rational approach, which can lead to appropriate treatment at the earliest and reduce mortality.

Introduction

Emergencies in thyroidology can present as relatively uncommon conditions which can be life threatening, but at the same time potentially reversible clinical entities, if picked up at the right moment. They are the natural outcome of either severe deficiency or excess of thyroid hormones. The deficiency of thyroid hormones may present as myxedema coma whereas decompensated thyrotoxicosis with the markedly raised thyroxine (T₄) and triiodothyronine (T₃) exceeding metabolic demands of the organism may present as fatal thyrotoxic storm. The basic understanding the differences of two entities (Thyroid storm Vs myxedema) and appropriate recognition and awareness of clinical sign and symptoms will lead to early diagnosis and better management ultimately leading to better outcome in these fatal disorders.

Thyroid Storm

Thyroid storm is a rare, life-threatening condition characterized by severe clinical manifestations of thyrotoxicosis. First described in 1926, still remains a diagnostic and therapeutic challenge for clinician.¹ The incidence of thyroid storm has shown a steady decline in the recent past, perhaps due to better awareness, early diagnosis and treatment of the primary condition leading to thyrotoxicosis thereby precluding its progression to the stage of acute crisis. Nevertheless, it may occur in 1% to 2% of hospital admissions for thyrotoxicosis.

Thyroid storm usually develops in a setting of a specific precipitating event such as surgery, infection, sepsis, trauma, cerebrovascular accident, drugs, an acute iodine load, or parturition. Thyroid storm may be the initial presentation of thyrotoxicosis in undiagnosed children especially in neonates. Clinical presentation includes hyperthermia, tachycardia, hyper tension, severe agitation and altered mental status. It is commonly seen in Graves’ disease but can also occur in other thyrotoxicosis conditions like toxic multi nodular goiter. Thyroid storm is almost invariably fatal if left untreated, hence rapid diagnosis and aggressive treatment is of paramount importance. No laboratory abnormality is specific to thyroid storm and the available scoring system is based on clinical criteria. The exact mechanisms of thyroid storm are poorly understood. A heightened response along with the increased availability of free hormones has been postulated. In addition to specific therapy directed against the thyroid, supportive therapy in an intensive care unit (ICU) and recognition and treatment of any precipitating factors is essential, since the mortality rate of thyroid storm is substantial.

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**Risk factors and pathogenesis of Thyroid storm**

Thyroid storm is commonly seen in patients with long-standing untreated hyperthyroidism (Graves’ disease, toxic multinodular goiter, solitary toxic adenoma). Rarely thyroid storm may develop secondary to sub acute thyroiditis or factitious thyrotoxicosis caused by excessive thyroxine intake. It is usually precipitated by an acute event such as thyroid or non-thyroidal surgery, trauma, infection, extreme weather, metabolic disturbances, drugs an acute iodine load, or parturition.

The precise pathogenesis of thyroid storm has not been defined but it has been hypothesized that a rapid rate of increase in serum thyroid hormone levels, increased responsiveness to catecholamines, or enhanced cellular responses to thyroid hormone are the main contributing factors. Thyroid hormones levels are found to be elevated in myriad of patients during storm, but a value does not differ significantly from those with uncomplicated thyrotoxicosis. An increase in free thyroid hormone levels has been proposed as causative of storm. But storm has occurred even in the absence of elevated free thyroid hormones levels.

Adrenergic hyperactivity due to altered interaction between thyroid hormones and catecholamines has also been suggested, but the exact role of catecholamines in storm awaits further study.

**Clinical features**

Earliest signs include fever, tachycardia, diaphoresis, increased CNS activity and emotional lability. If left untreated a hyperkinetic toxic state ensues in which symptoms are intensified. Progression to congestive heart failure, refractory pulmonary edema, circulatory collapse, coma and death may occur within 72 hours.

Central nervous system disturbances occur in 90% of patients. As the storm evolves and intensifies the CNS dysfunction may stimulate as encephalopathy, which may progress to include increasing agitation, emotional lability, confusion, paranoia, psychosis and ultimately coma. There has been case reports of patients of thyroid storm presenting as status epilepticus, stroke and even bilateral basal ganglia infarction. Cerebral sinus thrombosis has been reported more frequently in severe hyperthyroidism and therefore physicians treating thyroid storm should keep high index of suspicion in patients of thyroid disease presenting with neurological symptoms. Paralysis in a patient with thyroid storm can occur secondary to either stroke or rarely due to thyrotoxic periodic paralysis with hypokalemia, more frequently seen in Asian populations.

Cardiovascular abnormalities are seen in 50% of patients regardless of underlying heart disease. The most common manifestation includes rhythm disturbances, which may include tachyarrhythmia’s (sinus tachycardia, atrial fibrillations, supra-ventricular tachycardia or ventricular tachycardia), which may occur even in previously normal heart. Death in young patients with normal heart due to cardiovascular collapse from congestive heart failure (CHF) and hypotension has also been reported. Congestive heart failure or a reversible dilated cardiomyopathy also may be present even in young or middle-aged patients without known antecedent cardiac disease. A high-output state develops in thyrotoxicosis due to fluid overload attributable to excessive activation of the renin-angiotensin-aldosterone axis and also reduced afterload due to direct smooth muscle relaxing effect on vessels, leading to clinical presentation of systolic hypertension with widened pulse pressure. The characteristic feature of the hyperthyroid heart is its high myocardial oxygen demand, which may lead to acute coronary syndrome even in young patients.

Gastrointestinal Manifestations commonly presents as diarrhea and vomiting, which can aggravate volume depletion, postural hypotension, and shock with vascular collapse. The diffuse abdominal pain due to neurohormonal dysregulation or delayed gastric emptying may present as acute abdomen but sometime surgical obstruction can be a presentation in thyrotoxicosis. Rarely patient may present with liver dysfunction, jaundice and hepatic failure. Increased levels of serum alkaline phosphatase are also observed, predominantly because of increased osteoblastic bone activity in response to the augmentation of bone resorption. The jaundice in thyrotoxicosis is a poor prognostic marker and needs to be managed with immediate and vigorous treatment of the primary condition. As carbimazole as well as propylthiouracil, both are hepatotoxic drugs therefore treating these patients with hepatic dysfunction needs experience and critical judgment. Lithium, iodine therapy, cholestyramine or plasmapheresis may be life saving in these patient’s with acute hepatic failure.

**Laboratory and Hematological finding**

Elevated T₄ (thyroxine) and T₃ (triiodothyronine) levels and low TSH levels, are the common finding but the degree of thyroid hormone excess typically is not more profound than that seen in patients with uncomplicated thyrotoxicosis. A moderate leukocytosis is commonly seen in these patients even in the absence of any infection. Hyperthyroidism may be associated with hypercoagulability caused by increased concentrations of fibrinogen, factors VIII and IX, tissue plasminogen activator inhibitor 1, von-Willebrand factor, red blood cell mass increases secondary to erythropoietin stimulation, there is increased tendency of platelet plug
Major thromboembolic phenomenon may be responsible for up to 18% of deaths in patients of thyrotoxicosis. Other laboratory abnormalities may include a modest hyperglycemia without previous diabetes, probably as a result of augmented glycogenolysis and catecholamine-mediated inhibition of insulin release, as well as increased insulin clearance and insulin resistance. In prolong thyrotoxicosis cases the glycogen deposits in liver gets totally depleted leading to hypoglycemia in elderly, malnourished and acute abdomen patients who present with vomiting, abdominal pain and poor intake. Hepatic dysfunction in thyroid storm results in elevated levels of liver enzymes, transaminase, serum lactate dehydrogenase, and serum bilirubin.

**Diagnosis**

The diagnosis of thyroid storm is predominantly a clinical one and the laboratory findings of raised T3 and T4 may not be much different than those observed in uncomplicated hyperthyroidism. In few cases, even serum total T3 levels may be within normal limits, as in these patients T4 to T3 conversion is reduced due to some underlying conditions or illness as seen in sick euthyroid syndrome. Therefore, there are no universally accepted criteria or validated clinical tools for diagnosing thyroid storm. In 1993, Burch and Wartofsky et al. introduced a scoring system (Table 1) using precise clinical criteria for the identification of thyroid storm. A score of 45 or more is highly suggestive of thyroid storm, whereas a score below 25 makes thyroid storm unlikely. A score of 25 to 44 is suggestive of impending storm. This scoring system lacks specificity. The decision to initiate treatment is based on clinical judgment.

**Table 1: Burch and Wartofsky diagnostic criteria for thyroid storm**

<table>
<thead>
<tr>
<th>Thermoregulatory dysfunction</th>
<th>Scoring points</th>
<th>Cardiovascular dysfunction</th>
<th>Scoring points</th>
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<td>Temperature (°F)</td>
<td></td>
<td>Tachycardia</td>
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<td>99-99.9</td>
<td>5</td>
<td>99-109</td>
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<td>100-100.9</td>
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<td>110-119</td>
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<td>102-102.9</td>
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<tr>
<td>&gt; 104</td>
<td>30</td>
<td>&gt;140</td>
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**CNS effects**

| Mild                         | 10             | Atrial fibrillation        | 10             |
| Agitation                    | 20             | Heart failure              |                |
| Delirium                     |                |                            |                |
| Extreme lethargy             |                |                             |                |
| Severe                       | 30             |                               |                |
| Seizure                      |                |                             |                |
| Coma                         |                |                             |                |

**Gastrointestinal-hepatic dysfunction**

| Moderate                     |                |                             |                |
| Diarrhea                     |                |                             |                |
| Nausea/vomiting              |                |                             |                |
| Abdominal pain               |                |                             |                |
| Severe                       | 20             | Unexplained jaundice        |                |

**Heart failure**

| Mild                         | 5              |                            |                |
| Pedal edema                  |                |                             |                |
| Moderate                     | 10             | B/L basilar rales          |                |

| Severe                       | 15             | Pulmonary edema            |                |
| Seizure                      |                |                             |                |
| Coma                         |                |                             |                |

Thyroid storm is a real challenge. A multipronged management approach is recommended which is based on usage of different drugs acting through different pathways and by different mechanisms. The foremost target of treatment should be with specific antithyroid drugs to reduce the increased thyroid hormone production and reduce serum T4 and T3 hormone levels. The second line of action should be to control or block effects of excessive circulating thyroid hormones (free T4 and T3) in blood. This should be followed by a third component, which involves treatment of any systemic de-compensation, for example, congestive heart failure, and shock. And finally the fourth component should look for any underlying precipitating illness such as infection or ketoacidosis.

1. Therapy directed to the thyroid gland: Thyroid hormone synthesis is inhibited by the administration of thionamide anti-thyroid drugs, such as carbimazole, methimazole, and propylthiouracil. These drugs need to be given by nasogastric tube or per rectum as enema/ suppositories in comatose or uncooperative patient. Thionamides block new thyroid hormone synthesis within 60-120 minutes of administration but do not have any effect on the already released thyroid hormone or preformed hormone in blood. According to the recently published guidelines by the American Thyroid Association and the American Association of Clinical Endocrinologists, propylthiouracil (PTU) can be started with a loading dose of 500mg-1000mg followed by 250 mg every 4 hours, and methimazole should be administered 20 mg orally every four to six hours. Propylthiouracil may also block peripheral conversion of T4 to T3, and there is some evidence that over the first few hours after
administration, PTU reduces serum T₃ concentrations more rapidly than methimazole, whereas methimazole has some immunosuppressive effects also and is less hepatotoxic. Albeit there are no data showing that patients do better clinically with one thionamide over another, PTU is preferred for acute treatment of thyroid storm.

Iodine therapy complements the effects of thionamide therapy by blocking the release of stored hormone, a phenomenon called as Wolff-Chaikoff effect. The administration of iodine should be delayed for at least one hour after thionamide administration to prevent the iodine from being used as a substrate for new hormone synthesis. Available iodine formulations like Lugol’s iodine, SSKI can be used (5 drops orally every 6-8 hourly). Iodinated radiocontrast agent - Iopanoic acid and other iodinated radiocontrast agents block T₄ to T₃ conversion and inhibit thyroid hormone binding on cellular receptor. They have been extremely useful in treating severe hyperthyroidism and in preparing hyperthyroid patients for urgent surgery, and can be used at a dose of 0.5-1 g once daily.

2. Therapy to block Thyroid hormone action: When serum levels of T₃ and T₄ are very high in severe thyroid storm the anti-thyroid drugs may be inadequate. In these circumstances urgent plasmapheresis, therapeutic plasma exchange and peritoneal dialysis can be life saving, as they can reduce T₄ and T₃ levels within 36 hours. Intravenous albumin and fresh frozen plasma solution given during therapeutic plasma exchange provide new binding sites to reduce circulating levels of free thyroid hormones. Although the effect of plasma exchange is transient, it should always be supported by definitive therapy with anti-thyroid drugs or any other measures like early thyroidectomy. Surgical thyroidectomy has also been reported to reduce the mortality rate from about 20-40% under standard treatment to less than 10%. Beta-blocker’s are very effective in ameliorating the peripheral action of thyroid hormones and have immediate effect. Propranolol is frequently used for initial therapy because it can be given intravenously. However, it should be given under strict hemodynamic monitoring. Initial dose is 0.5 to 1 mg over 10 minutes followed by 1 to 2 mg over 10 minutes every few hours, can also be given orally or via nasogastric tube to achieve adequate control of heart rate, typically 60 to 80 mg orally every four to six hours. An alternative to propranolol therapy is a short acting beta-blocker esmolol, specially preferred in a critically ill patient in compensated shock or borderline blood pressure. A loading dose of 250 to 500 mcg/kg is given, followed by an infusion at 50 to 100 mcg/kg per minute. This regimen permits rapid titration of the dose of the drug to achieve adequate beta blockade while minimizing adverse effects. If there is a contraindication to use of beta-blocker, diltiazem can be used at 60-90 mg orally every 6-8 hours.

Glucocorticoids are another important medications characterized by a high therapeutic potency and modest ability to inhibit peripheral conversion of T₄ to T₃. Drugs such as hydrocortisone also exert immunosuppressive effect. Hydrocortisone, 300 mg initially followed by 100 mg intravenously every eight hours is routinely used in thyroid storm. The additional rationale behind the routine use of glucocorticoids is perhaps theoretical and unproven, but relates to possible relative adrenal insufficiency secondary to increased metabolic demands and more rapid turnover of cortisol.

Bile acid sequestrants may help by reducing thyroid hormone levels in thyrotoxic patients by interfering with enterohepatic circulation and recycling of thyroid hormone (e.g., cholestyramine 4 g orally four times daily). It is used as an adjuvant therapy in patients who cannot tolerate thionamide. Lithium can also be rarely used in case of contraindication or toxicities to anti-thyroid drugs (300 mg 8 hourly).

3. Therapy directed at systemic decompensation: Fluid replacement should be done in time as thyrotoxic patient’s are fluid depleted due to fever, diaphoresis, as well as by vomiting and or diarrhea and any delay may lead to vascular collapse. Judicious replacement of fluids is necessary in elderly patients with CHF or tachyarrhythmias. Intravenous fluids administration with 10% dextrose and appropriate electrolyte according to individual case scenario will help in better restoration of depleted hepatic glycogen store. Vitamin supplementation may also help in correction of any deficiency. Hypotension not readily reversed by adequate hydration may temporarily require inotropes and/or glucocorticoid therapy. Supportive therapy includes cooling measures, antipyretics, fluid and electrolyte correction. Avoid using salicylates as they can exacerbate thyrotoxic...
Myxedema Coma

Myxedema coma is a severe life threatening form of decompensated hypothyroidism with a high mortality rate commonly seen in elderly hospitalized females with untreated hypothyroidism, although it may occur in young as well as pregnant females too. Infections and noncompliance with thyroid supplements are the major precipitating factors. Fortunately, it is now a rare presentation of hypothyroidism, probably due to early diagnosis. Careful history and examination can reveal important clues regarding hypothyroidism and precipitating events in a poorly responsive patient. Early recognition and treatment are consequential. Timely intervention in a hypothyroid patient developing sepsis and other precipitating factors may reduce morbidity and mortality associated with myxedema coma. Treatment should be started on the basis of clinical suspicion without waiting for laboratory results.

Etiopathogenesis of Myxedema Coma

Myxedema coma is 4 to 8 times more common among women. It can result from any of the usual causes of hypothyroidism, particularly chronic autoimmune thyroiditis, usually precipitated by an acute event such as infection, myocardial infarction, cold exposure, or the administration of diuretics and sedative drugs, especially opioids. In a study by Dutta et al they have shown that nearly half of their patients had been treated with diuretic for edema. A commonly ignored background factor in myxedema crisis is the discontinuation of thyroid supplements in critically ill patients. It has been also reported in patients with secondary hypothyroidism, in some series 5%-15% of cases have been found to be due to hypothalamic or pituitary disease. There are also few case reports of its occurrence in patients with lithium or amiodarone induced hypothyroidism.

Markedly reduced intracellular T₃ due to hypothyroidism is the basic underlying pathology in myxedema coma, which causes hypothermia and suppression of cardiac activity. Decreased central nervous system sensitivity to hypoxia and hypercapnia leads to respiratory failure. Pleural effusion and generalized swelling may occur due to altered vascular permeability. Markedly reduced thyroid hormone may lead to reduced glomerular filtration rate (GFR), decreased water and solute delivery to distal nephron as well as secondary to increased vasopressin secretion.

Clinical presentation

While dealing with myxedema coma a detailed history focusing on precipitating factors like infection, drug intake, discontinuation of thyroxine medication, thyroid surgery and radioactive iodine ablation are paramount. The term myxedema coma is a misnomer, as quite a few patients are obtunded, rather than frankly comatose.

The two hallmark features of myxedema coma are decreased mental and profound hypothermia, but hypotension, bradycardia, hyponatremia, hypoglycemia, and hypoventilations are often present as well. Physical examination findings like dry skin, sparse hair, a hoarse voice, hypothermia, delayed tendon reflexes, macroglossia, non-pitting edema, goiter may be present.

The hypoxemia is a frequent development in myxedema coma. It’s primarily due to hypoventilation secondary to depressed hypoxic respiratory drive and a depressed ventilatory response to hypercapnia. Other contributing factors are obstruction of the upper airway caused by edematous tongue and vocal cords, as well as due to pleural effusion and ascites, which are commonly associated with this condition.

Confusion with lethargy and obtundation are the prominent neurological features, focal or generalized seizures may occur, due to concomitant hyponatremia, and status epilepticus has also been reported. Patients with severe hypothyroidism are at higher risk of developing shock and fatal arrhythmias. Cardiovascular involvement with bradycardia, decreased myocardial contractility, a low cardiac output, pericardial effusion and hypotension are other common features. Sinus
bradycardia, low voltage complexes, bundle branch blocks, complete heart blocks, and nonspecific ST-T changes are the prominent ECG findings. Patient may have normocytic or macrocytic anemia along with bleeding manifestations with elevated PT and APTT. Acquired Von-Willebrand disease has also been reported.39

Diagnosis

Diagnosis is based on history, examination and exclusion of other causes of coma. Patient with altered sensorium with hypothermia, with clinical and biochemical features of hypothyroidism in the setting of a precipitating factor, should be identified with a high index of suspicion and replacement therapy should be started as soon as possible. A diagnostic scoring system for myxedema has been proposed based on patients risk of myxedema coma, but its usefulness is limited by the fact that it has been derived from a study involving very small number of patients.40 Physical examination in a suspected case may include bradycardia, macroglossia, hoarseness of voice, delayed reflexes, dry skin, general cachexia, hypoventilation, and hypothermia, commonly without shivering. Laboratory evaluation may indicate hypoxemia, raised CO2, anemia, hyponatremia, hypercholesterolemia, and increased serum lactate dehydrogenase (LDH) and creatine kinase. On Cerebrospinal fluid analysis there may be high pressure with raised protein content. Most patients with myxedema coma have primary hypothyroidism, with high serum TSH and low free T4 values. On the other hand, a normal or low serum TSH value in a patient with a low free T4 value indicates central hypothyroidism.

Treatment

Myxedema coma is a true endocrine emergency and should be treated aggressively in an intensive care setting. Treatment should be instituted in patients with presumed myxedema coma without waiting for laboratory confirmation.

Treatment can be divided into:

1. Intensive care treatment with airway and ventilation support.
2. Thyroid hormone replacement therapy.
3. Hypothermia management
4. Hyponatremia management
5. Hypotension management

1. Airway and ventilation support in Intensive care: The hypoventilation, hypercarbia and respiratory acidosis lead to deep coma in myxedema patients. The airway management becomes one of the most important parts of critical care management, as respiratory failure is one of the common causes of mortality. Assisted mechanical ventilation is required for 1-2 days in most cases but in instances the mechanical ventilator may be required for days to weeks. The Hypoxemia is difficult to manage due to ventilation perfusion mismatch, therefore patient should be kept on mechanical ventilation for longer period and weaning should be tried after patient regains complete sensorium.41

2. Thyroid hormone therapy: Thyroid hormone replacement therapy is one of the most controversial aspects of myxedema management, due to paucity of good control trials of comparing the efficacy of various regimen and obvious difficulty in doing proper trials. There is still no consensus on oral versus intravenous T4/T3 and how to give it (dose, bolus, nasogastric or intravenous preparation). The optimum therapy should balance the need for quickly attaining physiologically effective thyroid hormone levels in the serum against the risk of precipitating a fatal tachyarrhythmia or acute coronary syndrome. T4 provides a steady, smooth, and slow onset of action with relatively few adverse events it is given intravenously in a loading dose of 200 to 400 mcg followed by a daily dose of 1.6 mcg/kg thereafter.42 Oral administration of T4 through nasogastric tube has proved to be equally effective, with a drawback that gastric atony may prevent absorption and put the patient at risk for aspiration. However, T3 is the active hormone in the body, and in a setting of severe illness there may be a decreased conversion of T4 to T3. Simultaneous T3 is administered in a dose of 5 to 20 mcg, followed by 2.5 to 10 mcg every eight hours for 1 or 2 days, and continued till the time the patient is alert enough to continue therapy through oral route. The single intravenous bolus of T4 was popularized by reports suggesting that replacement of the entire estimated pool of extra thyroidal T4 (usually 300–600 mcg) was desirable to restore near-normal hormonal status.42 This initial loading dose is followed by the maintenance dose of 50 to 100 mcg given daily (either intravenously or by mouth if the patient is adequately alert). Advantage of treatment with higher doses of T4 is still unproven and probably it may be more dangerous.43 Instead there are reports of improved outcomes with even lower doses of T4.44

The T4 to T3 conversion rate is somewhat reduced in systemic diseases (sick euthyroid syndrome or low T3 syndrome),45 hence T3 generation may be reduced in myxedema coma as a consequence of any associated illness (sick hypothyroid
syndrome). Considering this theoretical possibility, some endocrinologist suggest that small amount of T3 supplements should be prescribed with T4 treatment in the initial phase of thyroid storm, especially when associated with any systemic comorbid illnesses (sick euthyroid syndrome) as the conversion of T4 to T3 is reduced.\(^{45}\) When treatment is started with intravenous T3 alone, it should be started with 10 mcg every 4 hourly on day 1 and then the doses should be tapered to 10 mcg every 6 hourly on day 2 and day 3, in most instances by day 4 patients start tolerating oral medicine. The advantage of using T3 hormone is its quicker onset of action compared to T4 hormone, the rise in body temperature and increase in oxygen consumption may be seen within 2-3 hours of use of intravenous T3 while the same changes may take up to 8-14 hours after intravenous T4 therapy. The use of T3 may also be advantageous as it crosses blood brain barrier more rapidly as compared to T4 therefore may have more positive effects in patients suffering from neuropsychological symptoms and coma during myxedema.\(^{46}\)

The negative side of intravenous T3 treatment is its large unpredictable fluctuation in its serum levels and also higher serum levels which may lead to fatal outcomes, especially cardiac mortalities.\(^{47}\) Considering various risk and benefit of only T4 vs only T3 hormone treatment regimen, there lies an intermediate or combined (T4+T3) regimen pathway. The rational behind this combined therapy approach is to provide combination of T4 and T3.\(^{48}\) In this regimen the intravenous T4 dose of 4mcg/kg lean body weight (or approximately 200–300 mcg) is given with a bolus dose of 10 mcg of intravenous T3. After this an additional single intravenous dose of 100 mcg T4 is given on day two with 20-30 mcg of intravenous T3 in divided doses. The T3 should be continued at the same dose of 10 mcg twice or thrice a day till patient regains consciousness and start accepting orally, while the T4 should be continued at maintenance dose of 50 mcg per day by intravenous or oral depending on the consciousness and oral acceptance.

3. Hypothermia management: The body temperature can be restored with treatment with thyroid hormone replacement. Simultaneous use of warming measures, such as warm blankets and increasing the room temperature with heater can be used as additional interventions to keep the patient warm until the thyroid hormone effect is achieved. Too aggressive warming should be avoided, as it may be deleterious to patient’s health secondary to peripheral vasodilation, leading to hypotension and shock.

4. Hyponatremia management: Patient with hyponatremia are prone to develop seizures and coma even in euthyroid state, in myxedema crisis this hyponatremia may further contribute to comatose state. The mortality of severe hyponatremia (105-120 mmol/L) is manifold higher in myxedema patients. The appropriate management of severe hyponatremia is slightly tricky in these patient and need close monitoring of serum sodium after correction with hypertonic saline followed by rapid diuresis with loop diuretics. This often require administration of 50–100 mL of 3% sodium chloride, initially to increase serum sodium concentration by about 2 mmol/L early in the course of treatment, followed by an intravenous bolus furosemide (40 to 120 mg) to promote a water diuresis.\(^{49}\) A small, quick increase in the serum sodium concentration by 2–4 mmol/L in severe hyponatremaic patient may be effective in improving sensorium because even a slight reduction in brain swelling results in a substantial decrease in intracerebral pressure (ICT).\(^{50}\) On the other hand, too rapid correction of hyponatremia can cause a dangerous complication, the osmotic demyelination in the form of central pontine myelinoisis.

In patients with chronic hyponatremia, the serum sodium correction should be <10 to 12 mmol/L in 24 hours and less than 18 mmol/L in 48 h. After achieving a serum sodium level of >120mmol/L restriction of fluids may be good enough to correct hyponatremia. But patient with cardiovascular disease may need close monitoring of volume status with central venous pressure monitoring. The intravenous vasopressin antagonist, conivaptan can be effective medicine in treating hyponatremia in hypothyroid patients as high vasopressin levels has been documented in Myxedema coma patients.\(^{51}\) The Conivaptan is approved by US FDA and the recommended dose is 20 mg of loading dose, to be infused over 30 minutes followed by 20 mg/day of continuous infusion for up to 4 days. Unfortunately, at present no data are available on the use of conivaptan in severe hyponatremia (<115 mEq/L) in hypothyroidpatients.\(^{52,53}\)

5. Hypotension: Hypotensive myxedema patients may require additional volume-repletion therapy in spite of corrected
T3/ T4 replacement to correct volume status. Fluids maybe administered cautiously as 5% to 10% dextrose in N/2 sodium chloride if hypoglycemia is present, or as isotonic normal saline if hyponatremia is present. An agent such as dopamine might be used to maintain coronary blood flow, but patients should be weaned off the vasopressor as soon as possible because of the risk of an inotropes induced iatrogenic ischemic event. Hypocortisolemia may be due to primary or secondary adrenal insufficiency. Thyroid hormone replacement may increase cortisol clearance and may aggravate cortisol deficiency. Patient must be treated with glucocorticoids in stress doses (e.g., hydrocortisone given intravenously, 100 mg every eight hours).

Summary

Thyroid storm and myxedema coma are two major life-threatening thyroid emergencies encountered in endocrinology clinical practice. The diagnosis of both requires high index of clinical suspicion and early appropriate treatment can markedly reduce mortality. In thyroid storm in spite of accurate diagnosis and high fatality has been documented in literature. While Myxedema fatality has markedly decreased with advances in intensive care management. The key to successful management of these emergencies is timely diagnosis and management by experienced physician in an intensive care setting.

References

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