Thyrotoxicosis

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Introduction

The term thyrotoxicosis refers to the clinical syndrome of hyper metabolism and hyperactivity those results from excessive quantities of the thyroid hormones. The term hyperthyroidism is used to denote sustained increased in thyroid hormone biosynthesis and secretion by the thyroid gland. While many patients with thyrotoxicosis have hyperthyroidism, it is not so in others such as - those in whom it is caused by thyroiditis or exogenous thyroid hormone administration. Thyrotoxicosis can range in severity from subclinical hyperthyroidism to life threatening thyroid storm. Although we do not have prevalence data, thyrotoxicosis is found in various age groups (children, elderly) and in different clinical situations.

Aetiology of Thyrotoxicosis

The most common cause of thyrotoxicosis is Grave's disease followed by toxic multinodular goiter (TMNG), solitary toxic adenoma and thyroiditis. The other less common causes include TSH secreting pituitary adenoma, struma ovarii, metastatic functional differentiated thyroid cancer and metatstatic tumors within the thyroid gland causing destruction induced thyrotoxicosis (Table 1)

Pathogenesis of Thyrotoxicosis

Grave's Disease: Grave's disease is the commonest cause of thyrotoxicosis being more common in females than males. It is caused by an activating antibody which targets the TSH receptor of the thyroid follicular cells and stimulates thyroid hormone production, increase thyroid vascularity and growth similar to thyrotropin, but without normal feedback inhibition.

The TSH-R antibodies also bind to the retro-orbital tissues producing a T-cell inflammatory response, release of cytokines, activation of fibroblasts and accumulation of glycosaminoglycans leading to an infiltratory ophthalmopathy. A small percentage of these patients with ophthalmopathy have a similar process of activation of dermal fibroblasts in the anterior leg leading to the development of a pretibial myxoedema.[1]

Toxic multinodular goiter (TMNG) is the second leading cause of thyrotoxicosis and is more common in our country as compared to other regions. It generally arises in a multinodular thyroid gland that subsequently develops autonomously functioning nodules over time. It is more prevalent in populations with greater iodine deficiency. TMNG develops in older individuals, with a longstanding previous multinodular goiter in which one of the nodules attains functional autonomy. Several different mechanisms could contribute to this process. One of the common mechanisms being somatic mutation in the TSH receptor gene leading constitutive receptor activation and upregulation of the cAMP signaling, has been described in upto 60% of these patients.

Toxic adenoma: The solitary toxic adenoma causes hyperthyroidism in slightly younger individuals and also results from a similar process of constitutive activation of the TSH receptor due to mutations in the TSH receptor gene. The course of the disease evolves similar to that of the TMNG with the nodule autonomy developing after the nodule has been present for a considerable period of time.[2]

Table 1 : Causes of Thyrotoxicosis

Primary hyperthyroidism
Graves' disease
Toxic multinodular goiter
Toxic adenoma
Functioning thyroid carcinoma metastases
Activating mutation of the TSH receptor
Activating mutation of G_{sa} (McCune-Albright syndrome)
Struma ovarii
Drugs: iodine excess (Jod-Basedow phenomenon)
Thyrotoxicosis without hyperthyroidism
Subacute thyroiditis
Silent thyroiditis
Other causes of thyroid destruction: amiodarone, radiation, infarction of adenoma
Ingestion of excess thyroid hormone (thyrotoxicosis factitia) or thyroid tissue
Secondary hyperthyroidism
TSH-secreting pituitary adenoma
Thyroid hormone resistance syndrome: occasional patients may have features of thyrotoxicosis
Chronic gonadotropin-secreting tumors
Gestational thyrotoxicosis
Thyrotoxicosis factitia

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Clinical features of thyrotoxicosis (Table 2)

Subclinical hyperthyroidism is defined by normal circulating levels of free T_4 and T_3 and low levels of TSH. It is caused by the same conditions that account for the majority of cases of overt hyperthyroidism i.e. Graves' disease, toxic multinodular goiter, and solitary functioning thyroid nodules. Subclinical hyperthyroidism is associated with an increased risk of atrial fibrillation and mortality, osteopenia/osteoporosis in postmenopausal women and mild hyperthyroid symptoms. Thyrotoxicosis results in a hypermetabolic state with energy production exceeding the energy expenditure leading to increased heat production presenting as heat intolerance perspiration and fever. Even though there is greater energy expenditure there is generalized weakness and fatigue

Table 2: Clinical features of thyrotoxicosis

Symptoms	Signs
Hyperactivity, irritability, dysphoria	Tachycardia; atrial fibrillation in the elderly
Heat intolerance and sweating	Tremor
Palpitations	Goiter
Nervousness, fatigue and weakness	Warm, moist skin
Dysnoea	Muscle weakness, proximal myopathy
Weight loss with increased appetite	Hyperreflexia
Diarrhea / Hyperdefecation	Lid retraction or lag
Polyuria	Gynecomastia
Oligomenorrhea	Loss of libido

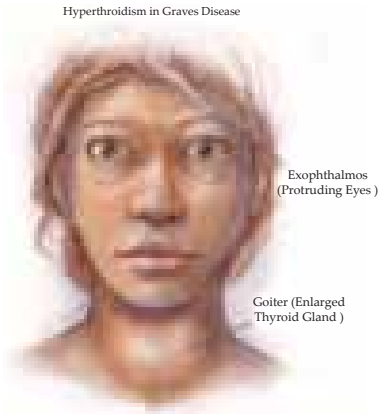

Fig 1: Hyperthyroidism

attributable to the associated myopathy.

The thyroid hormones exert their effects on heart by altering functions of sodium, potassium and calcium channels leading to increased cardiac contractility and cardiac output. They also influence the production of several cardiac muscle proteins. Tachycardia and palpitations are the commonest symptoms with the finding of a strong apical impulse, pulse pressure and a hyperdynamic precordium. Rubbing of the hyperdynamic precordium against the pleura may produce the 'Means-Lerman scratch', sometimes heard in these patients. Chest pain can also be produced due to increased myocardial oxygen demand, coronary artery spasm leading to frank coronary ischemia.[4]

Increased frequency of bowel movements can result from increased motor contraction of small bowel, leading to a rapid transit of intestinal contents. Thyrotoxicosis can lead to neuropsychiatric changes resulting in restlessness agitation, emotional lability, psychosis and even coma. Behavioural studies reveal poor performance in memory and concentration testing proportional to the degree of thyrotoxicosis. Thyroid hormones influence the GnRH signalling causing disruption of normal LH, FSH pulsatility, thereby leading to menstrual irregularity. There is an increase in SHBG levels which leads to decreased metabolic clearance of estradiol and an increase in conversion of androstenedione to estrone and estradione. These changes may produce symptoms of decreased libido, gynecomastia and spider angiomata in roughly 10% of male patients with thyrotoxicosis.[5] Elderly individuals with thyrotoxicosis can however have masking of the typical hyperadrenergic symptoms either due to underlying disorders such as an autonomic neuropathy or due to concomitant medications such as β-blockers and may present with a form of 'Apethetic hyperthyroidism' characterised by significant weight loss, weakness, dizziness and memory loss and physical findings of sinus tachycardia or atrial fibrillation. The clinical findings are summarized in table 3. The clinical manifestations of thyrotoxicosis are independent of its cause. However, certain features of this disorder like the duration of thyrotoxicosis, size and shape of the gland, presence or absence of extra thyroidal manifestations vary with the underlying etiology and may provide clues to this.

Unique clinical features of thyrotoxicosis as seen in India

Indian patients with thyrotoxicosis have been observed to present with more severe weight loss leading to emaciation, dyspnea, proximal muscle weakness, diarrhoea / hyperdefecation (Fig. 1). Prevalence of anaemia is more common leading the frequent presentation with arrhythmias and congestive cardiac failure, so also is the presence of hepatic dysfunction and cortisol deficiency.

Table 3 : Clinical manifestations of specific causes of thyrotoxicosis

Clinical findings	Cause
Diffuse goiter	Grave's disease, silent thyroiditis
Uninodular goiter	Thyroid autonomy
Multinodular goiter	Thyroid autonomy
Impalpable thyroid gland	Exogenous thyroid hormone
Thyroid pain and tenderness	Subacute thyroiditis
Ophthalmopathy	Grave's disease
Localized dermopathy	Grave's disease
Thyroid achropachy	Grave's disease

Laboratory diagnosis

Biochemical confirmation of thyrotoxicosis is based on the finding of a suppressed TSH (<0.05 μU/mL) in combination with elevated serum total or free T_4 and T_3 levels in patients with clinically evident thyrotoxicosis. Although a TSH assessment alone may be appropriate for routine screening in an asymptomatic patient, the suspicion of thyrotoxicosis warrants the additional assessment of $T_4$and T_3. In cases in which subclinical hyperthyroidism is suspected, TSH measurement may be used as a first diagnostic step, with subsequent T_4 and T_3 assessment if TSH is suppressed. Laboratory measurement of total T_3 and total T_4 reflects mainly protein-bound hormone concentrations. There are several conditions altering the protein binding of T_4. (Table 4) These protein-binding abnormalities affect the index tests (free T_4 index and free T_3 index) and may give inaccurate values when changes in protein binding are present. For these reasons, free T_4 assays are preferred over the total hormone estimation and index tests; however their availability may not be universal.[5] The ratio of T_4 to T_3 frequently has a characteristic pattern in different thyrotoxic states. Evaluation of the T_4/T_3ratio may be a useful tool in the initial diagnosis of thyrotoxicosis when radioactive iodine uptake testing is not readily available or is contraindicated. Graves' disease and toxic nodular goiter typically present with increased T_3 production, with a T_3/T_4 ratio greater than 20. With thyrotoxicosis caused by thyroiditis, iodine exposure, or exogenous levothyroxine intake, however, T_4 is the predominant hormone and the T_3/T_4 ratio is usually less than 20. A small number of thyrotoxic patients may present with an increase in serum free T_3 and normal T_4. This is referred to as "T_3 toxicosis".

Thyroid antibodies: Although the antithyroid peroxidise and anti-thyroglobulin antibodies may be elevated in almost all cases of thyrotoxicosis, measurement of the TSH-R antibodies may be helpful in the diagnosis and management of Grave's disease in certain situations. It may be helpful in prediction of post-partum Graves' disease and neonatal thyrotoxicosis. It has also been used to predict chances of relapse in patients treated with antithyroid medications and in the identification of orbitopathy in the absence of obvious features of thyrotoxicosis.[6]

Other laboratory abnormalities in thyrotoxicosis

Thyrotoxicosis may also cause hyperglycemia, hypercalcemia, elevated alkaline phosphatase, leukocytosis, and elevated liver enzymes. The hyperglycemia is typically mild and is caused by catecholamine-induced inhibition of insulin release and increased glycogenolysis. Mild hypercalcemia and elevated alkaline phosphatase occur as well because of direct TSH stimulation of osteoblastic bone resorption mediated by the NF-kB-RANKL pathway.

Table 4: Causes of elevated serum thyroxine concentrations

Thyrotoxicosis
Increased Serum protein binding
Increased serum thyroxine-binding globulin concentrations
Inherited
Estrogens: pregnancy, exogenous, tumoral production
Hepatitis, hepatoma
HIV infection
Carcinoma of pancreas, hepatoma
Psychiatric and Medical Illness
Drugs
Methadone, heroin, clofibrate, 5-flurouracil
Familial dysalbuminemic hyperthyroxinemia
Increased serum transthyretin binding or concentrations
Propranolol (high doses)
Amiodarone
Radiographic contrast agents used for cholecystography
Anti-T_4 immunoglobulins

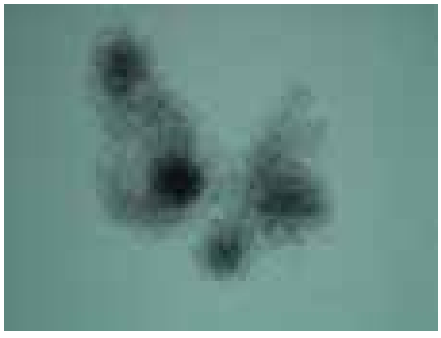

Fig. 2 : Nuclear scan in a patient with toxic multinodular goiter

Imaging

Different imaging modalities may assist in the determination of the etiology of thyrotoxicosis. The most important of these are the thyroid nuclear imaging studies and anatomic studies like thyroid ultrasound.

Nuclear medicine scanning

Radioactive iodine uptake and scanning is a very useful tool in the diagnostic evaluation of thyrotoxicosis. After ingestion of the tracer usually I^{131} or I^{123}, the emitted γ radiation allows external detection, calculation of fractional uptake and scintigraphic imaging of the thyroid gland. The uptake is measured at 6 hr and 24 hr and the normal values range between 5 – 15% for the 6 hr uptake and 5-25% for the 24 hr uptake. Technetium-99m (Tc-99m) pertechnetate imaging is preferably being used now, since it is actively trapped in thyroid follicular cells like iodine and has the advantage of a rapid turnover requiring the uptake and scan to be completed within 20-30 min with a much lower dose of radioactivity. However, it has limitations in terms of detecting organification defects.[7]

Thyroid ultrasonography in the evaluation of hyperthyroidism

Thyroid sonography may be useful in the diagnostic evaluation of thyrotoxicosis. Sonographic assessment can identify thyroid nodules and goiter that may not be readily apparent on examination. Additionally, sonographic Doppler flow assessment may provide particularly useful information about several thyrotoxic states. An index of blood flow per unit area has been used to distinguish between Graves' disease and thyrotoxicosis caused by non-hypermetabolic destructive thyroiditis. Using a thyroid blood flow area of 8% or greater had a sensitivity of 95% and a specificity of 90% for the prediction of Graves' disease. This may also be helpful in differentiating the

Table 5 : Shows the radiodine uptake and pattern of distribution in various disorders causing thyrotoxicosis

Cause of thyrotoxicosis	Fractional uptake in 24 hr (%)	Pattern of distribution of tracer in thyroid
Grave's Disease	35-95	Homogenous
Toxic nodular goiter (uni or multinodular)	20-60	Restricted to regions of autonomy
Subacute thyroiditis	0-2	Little or no uptake
Silent thyroiditis	0-2	Little or no uptake
Iodine-induced thyrotoxicosis	0-2	Little or no uptake
Factitious or iatrogenic thyrotoxicosis	0-2	Little or no uptake
Struma ovarii	0-2	Uptake in ovary
Follicular carcinoma	0-5	Uptake in tumor metastasis
TSH induced thyrotoxicosis	30-80	Homogenous

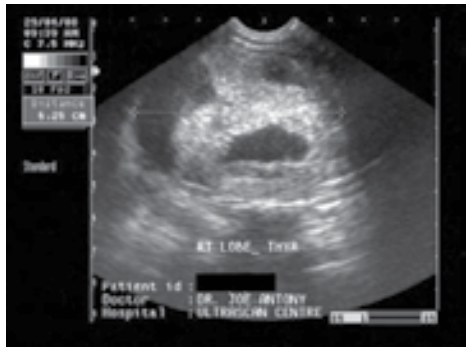

Fig. 3 : Ultrasonography showing multinodular goiter

two different forms of Amiodarone induced thyrotoxicosis (AIT).

Treatment of Thyrotoxicosis

The approach to treatment of thyrotoxicosis depends on the etiology of thyrotoxicosis and consists of the use of agents that block the synthesis of thyroid hormone in the thyroid gland, the generation of active T_3 from the pro-hormone T_4 or blocking its actions at the end organs.

Thionamides

The thionamides are the most commonly used agents which belong to two different categories, the imidazole derivatives – carbimazole and methimazole and the thiouracil derivative – propylthiouracil (PTU). The thionamides act by inhibing the thyroid peroxidase–mediated oxidation of iodide, iodine organification, and iodotyrosine coupling. Also, thionamides inhibit the thyroperoxidase-catalyzed coupling process through which iodotyrosine residues are combined to form T_4 and T_3. PTU also possesses the extrathyroidal action of blocking conversion of T_4 to T_3 in peripheral tissues through inhibition of type 1 deiodinase, which may be of benefit in cases of thyroid storm or severe thyrotoxicosis.

Methimazole and PTU have different pharmacologic properties that should be considered while making a choice of therapy. The serum half-life of methimazole is 6 to 8 hours, whereas the half-life of PTU is 1 to 2 hours. These short half-lives would suggest that the thionamides should be administered in divided daily doses. However, methimazole is effective even when given once daily, since it interferes with iodine organification more effectively by irreversibly inhibiting

thyroid peroxidase, compared to PTU which causes reversible inhibition and also a single dose of methimazole has been shown to provide measurable intrathyroidal concentrations lasting up to 20 hours.[8]

In addition to the effects on organification of thyroid hormones, thionamides have been shown to have an inhibitory effect on the immune system, In several in-vitro and in-vivo studies they have been shown to have important immunosuppressive effects such as decreasing immune related molecules such as intracellular adhesion molecule -1 and soluble interleukin-2 and also the TSH receptor antibodies. They have been shown to affect the intrathyroidal lymphocytes reducing the HLA Class II expression and promoting their apoptosis. Due to immunomodulatory effect of thionamides block and replace regimes have been used to provide continued immunosuppressive effect while preventing the development of hypothyroidism.

Adverse effects of thionamides

The common adverse effects of thionamides are abnormal sense of taste, pruritis, arthralgias and urticaria, occurring in about 1-5% of patients. Use of antihistaminics may be helpful for the pruritis and urticaria, while switching to another thionamide may also be helpful. However, in upto 50% of patients there may be cross-reactivity between methimazole, carbimazole and PTU. In such patients, discontinuation of thionamide therapy and preparation for definitive treatment with the use of alternative therapies may be helpful.[7,9]

Agranulocytosis is a potentially lethal adverse effect of thionamides which usually occurs in the first three months of therapy. Its occurrence is related to the dose of methimazole (generally occurring with doses greater than 30mg/day) and not of PTU. It can also in an idiosyncratic manner even late in the course of treatment. The incidence of agranulocytosis with methimazole and PTU is 0.2-0.5%. It presents with fever and sore throat progressing rapidly to sepsis. Any patient on thionamides presenting with fever and sore throat should be evaluated with complete blood counts to exclude this condition. Routine assessment of blood counts in patients receiving thionamides has not been shown to be useful and is hence not recommended. Hepatitis is another uncommon but serious adverse effect of thionamide therapy occurring in 0.1-0.2% of patients. Methimazole induced hepatotoxicity presents as a cholestatic process while PTU can produce an allergic hepatitis with markers of hepatocellular injury, which is more common in children. Vasculitis is another serious adverse affect which can occur rarely and often presents with arthritis, skin ulceration, vasculitic rash, sinsusitis, hemoptysis and acute renal insufficiency. Serological markers such as anitneutrophil cytosplasmic antibodies may also be present in such individuals. [10]

β adrenergic blocking drugs

β adrenergic blockers control the cardiovascular and hyperadrenergic manifestiations of thyrotoxicosis and are therefore useful adjuncts to the management of thyrotoxicosis. Propranolol is commonly used for this purpose. Some of the cardioselective β-blockers could be preferred in patients with bronchial asthma. There is also a rapid metabolism of propranolol in thyrotoxicosis hence larger doses are needed. In addition to the β blocking effect propranolol in doses greater than 160 mg/day decreases the T_3 generation by upto 30% by inhibiting the 5′-monodeiodinase enzyme. However this effect develops slowly over 7-10 days of treatment. β blockers have an adjunctive role in the alleviating of symptoms and are particularly useful during diagnostic evaluation and while awaiting the results of primary therapy and in patients with transient toxicosis due to thyroiditis where they form the primary therapy.

Other medications used for thyrotoxicosis

Several other medications can also be used in treatment of thyrotoxicosis due to either direct antithyroid effects or other actions. They are particularly useful adjuncts in management of severe thyrotoxicosis or when there are adverse reactions with the thionamides.

Iodine: Inorganic iodine has several mechanisms of action making it a useful agent for the management of thyrotoxicosis. At high concentrations it blocks the release of pre-stored hormone, decreases iodide transport, and prevents oxidation in the follicular cells. This inhibition of thyroid metabolism by iodine is called as the Wolf-Chaikoff effect and is only transient. The thyroid gland begins to start escaping from iodine inhibition after about 48 hours as the iodine transport system adapts to high concentrations of iodine by modulating the activity of the sodium iodine symporter, so that within 1-2 weeks complete escape from inhibition occurs. While treating thyrotoxicosis with iodine the addition of thionamides is essential to prevent aggravation of symptoms with the loss of Wolf-Chaikoff effect. The available oral preparations are Lugol's iodine (160mg/ml) used as 5 drops daily, SSKI (saturated solution of potassium iodide - 760 mg/ml) used as 1 drop daily, or collosol iodine The oral iodinated contrast agents iopanoic acid and sodium iodate have been used for the management of severe thyrotoxicois. They have additional effects of inhibiting the types 1 and 2 5′monodeiodinase and inhibition of T_3 and T_4 binding to the cellular receptors. [11]

Potassium perchlorate: Potassium perchlorate inhibits the iodine uptake by the thyroid gland by direct inhibition of the sodium iodine symporter. Potassium perchlorate is used orally in doses of 500mg twice daily. It can be combined with the thionamides which inhibit the organification and synthesis of thyroid hormones within the gland. Such a combination can rapidly normalize thyroid hormone levels in about 4 weeks.

Potential side effects of potassium perchlorate include aplastic anaemia and nephritic syndrome, which are particularly seen with the uses of higher doses and prolonged treatment. The use of this agent is therefore in the intial stages for about 1month with doses not greater than 1 gm /day in combination with the thionamides. It is particularly useful in patients with iodine –induced thyrotoxicosis as seen with amiodarone induced thyrotoxicosis.

Lithium: Lithium has several effects on thyroid function. It inhibits coupling of iodotyrosine residues that form iodothyronines (T_3 and T_4) and also decreases thyroid hormone release. It has to be administered in doses of 300mg q 8 hourly. It is particularly useful when thionamides are contraindicated due to adverse effects or toxicity and in other situations can also be combined with them. Lithium toxicity has to be avoided by monitoring the serum levels and maintaining them below 1mEq/L.

Cholestyramine: Thyroid hormones are metabolized in the liver by conjugation to sulphates and glucoronidases, which are subsequently excreted in the bile. However, a fraction of the conjugated hormone is deconjugated in the bowel and reabsorbed during enterohepatic circulation. The enterohepatic circulation of thyroid hormones is increased in thyrotoxicosis. Cholestyramine is an anion exchange resin that has been shown to decrease the reabsorption of thyroid hormones from the enterohepatic circulation. It has been found to be a useful

Table 6 : Situations favouring surgical therapy over radioactive iodine therapy for hyperthyroidism

Absolute indications
Suspicious of biopsy proven malignant nodules
Co-morbidity requiring surgery e.g. Hyperparathyroidism
Contraindication to radioactive iodine ablation
Pregnancy or lactation
Young children
Severe intolerance to antithyroid medications
Large compressive / obstructive goiter
Relative indications
Severe Grave's ophthalmopathy
Patients desiring pregnancy within 6-12 months of treatment
Patients unable to continue close follow up
Patients incompletely treated by radioactive iodine ablation

therapeutic agent in the management of thyrotoxicosis. It is administered orally at rate of 4g four times daily, in combination with methimazole of PTU, its has been found to cause a more rapid decline in thyroid hormone levels than thionamide therapy alone. [11,12]

Radioactive Iodine: Radioactive thyroid ablation is becoming the most widely used definitive treatment for thyrotoxicosis due to Grave's disease or toxic multinodular goiter. It has the advantage of allowing the discontinuation of the use of thionamides with worrisome side effects such as agranulocytosis, hepatotoxicity or vasculitis. The major long term side effect of radioactive iodine therapy is permanent hypothyroidism. Short term side effects include acute exacerbation of thyrotoxicosis, radiation thyroiditis presenting as anterior neck tenderness or gastritis and sialadenitis. Pre-treatment with thionamides has been shown to reduce the risk of post-treatment thyrotoxicosis. However the efficacy of radioactive iodine treatment may also be reduced. This is particularly true with PTU, whereas with methimazole and carbimazole this effect was not significant as long as these agents were discontinued 3-5 days before treatment.

The response to radioactive iodine is not immediate, usually requiring about 2-3 months. Most patients therefore require antithyroid medication to be continued for a few months until hypothyroidism develops. Persistence of hyperthyroidism beyond 6 months after therapy may require re-treatment with radioactive iodine to achieve complete ablation. One of the major concerns has been the risk of second malignancy after the use of radioactive iodine therapy particularly in children. These concerns have been with relation to the development of leukaemia or malignant lymphoma, thyroid cancer and cancers of the small bowel. This risk is shown to relatively small and not consistently demonstrated across all studies. The risk of thyroid malignancies is eliminated when an ablative approach to therapy is used with a goal to render the patient hypothyroid, with no significant residual functional thyroid tissue.

Management Strategies for Disorders Causing Thyrotoxicosis

Grave's Disease: Antithyroid medications to decreased thyroid hormone production along with β-blockers to control the peripheral manifestations of thyrotoxicosis form the mainstay of therapy. Once the patients is rendered euthyroid the options include continued use of antithyroid drugs for 12-18 weeks, or definitive treatment with radioactive iodine or surgery. In those who are continued on antithyroid medications smaller doses of 5-10 mg Methimazole or PTU at doses of 100-200 mg is sufficient. A few patients may need thyroxine supplementation to prevent hypothyroidism. After cessation of therapy a close follow up for 3-6 months is required to detect relapse, which may occur in as many as 50-60% of patients. In such a situation radioiodine treatment or surgery has to be considered. [13]

Radioactive treatment is generally effective and has very few adverse effects other than the development of hypothyroidism and hence is the preferred option for a definitive treatment. Surgical therapy consists of subtotal or near total thyroidectomy. There are certain situations in which the surgical option may be preferred (table 6) in preference to radioactive iodine.

Toxic multinodular goiter and solitary toxic adenoma

Although antithyroid medications can normalize thyroid functions, they do not provide a definitive therapy in these patients as there is an autonomous nodule function. Hence, radioactive ablation of the thyroid or thyroidectomy have to be employed after initial control of the disorder with antithyroid medications. Radioactive ablation may be the preferred mode of therapy but surgery may be chosen in certain situations as mentioned in table 6. The dose of radioactive iodine used is generally higher than that required for Grave's disease.

Thyrotoxicosis due to thyroiditis

The treatment of thyrotoxicosis in this situation is usually symptomatic and involves control of hyperadrenergic symptoms with β-blockade, management of pain is with the use of non-steroidal anti-inflammatory drugs. The β blockade may need to be continued for a few weeks. For severe pain persisting in spite of maximum nonsteroid therapy, prednisolone in doses of 40 mg/day may be used for 7-10 days followed by tapering doses for 1-2 weeks. A follow-up has to be maintained for the subsequent development of hypothyroidism.

Amiodarone induced thyrotoxicosis (AIT)

Type I AIT requires the use of thionamides and β blockers for mild to moderate disease, while more severe disease may require the addition of potassium perchlorate which blocks the activity of sodium iodine symporter, thereby inhibiting iodine uptake into the gland. When medical therapy is not effective, thyroidectomy should be considered. Type II AIT is however a destructive thyroiditis, has a self limiting course, but the more severe forms will improves well with the use of glucocorticoids. [14]

Conclusions

- The common causes of thyrotoxicosis are Grave's disease , toxic multinodular goiter (TMNG), solitary toxic adenoma and thyroiditis
- Symptoms of hyperthyroidism include hyperactivity, irritability, dysphoria, heat intolerance and sweating, palpitations, nervousness, fatigue and weakness, dyspnoea, weight loss with increased appetite, diarrhea / hyperdefecation , polyuria, oligomenorrhea and loss of libido
- Signs of hyperthyroidism include tremors, goiter, warm, moist skin muscle weakness, proximal myopathy, hyperreflexia, lid retraction or lag and gynecomastia
- Biochemical confirmation of thyrotoxicosis is based on the finding of a suppressed TSH (<0.05 μU/mL) in combination with elevated serum total or free T_4 and T_3 levels in patients with clinically evident thyrotoxicosis.
- Imaging modalities which assist in the determination of the etiology of thyrotoxicosis include thyroid nuclear imaging studies and thyroid ultrasound
- Treatment of thyrotoxicosis depends on the etiology of

thyrotoxicosis

- Medical management consists of antithyroid medications carbimazole , methimazole and– propylthiouracil to decreased thyroid hormone production along with β-blockers to control the peripheral manifestations of thyrotoxicosis
- In Graves's disease, radioactive treatment is effective and has very few adverse effects other than the development of hypothyroidism and hence is the preferred option for a definitive treatment. Surgical therapy consists of subtotal or near total thyroidectomy
- For toxic multinodular goiter and solitary toxic adenoma radioactive ablation of the thyroid or thyroidectomy have to be employed after initial control of the disorder with antithyroid
- The treatment of thyrotoxicosis due to thyroiditis is usually symptomatic and involves control of hyperadrenergic symptoms with β-blockade and management of pain with the use of non-steroidal anti-inflammatory drugs

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