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A REVIEW - THYROIDISM

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ABSTRACT

Hypothyroidism is a common condition in which the thyroid gland provides insufficient amounts of thyroid hormone for the needs of peripheral tissues. The most common cause in adults is chronic lymphocytic thyroiditis (Hashimoto thyroiditis), but there are many other causes. Because most of the clinical features of hypothyroidism are nonspecific, the diagnosis requires laboratory testing. Serum thyroid-stimulating hormone (TSH) measurement is the best diagnostic test; an elevated TSH level almost always signals primary hypothyroidism. Serum free thyroxine levels may be below the reference range (overt hypothyroidism) or within the reference range (subclinical hypothyroidism). All patients with overt hypothyroidism should be treated, but those with subclinical hypothyroidism do not always benefit from treatment, especially elderly patients and those with baseline TSH levels below 10 mU/L. Oral L-thyroxine is the treatment of choice because of its well-demonstrated efficacy, safety, and ease of use. Therapy goals are symptom relief and maintenance of serum TSH levels within the reference range. Myxedema coma is a life-threatening form of decompensated hypothyroidism that must be treated with aggressive L-thyroxine replacement and other supportive measures in the inpatient setting. Thyrotoxicosis has multiple etiologies, manifestations, and potential therapies. Appropriate treatment requires an accurate diagnosis and is influenced by coexisting medical conditions and patient preference. This article describes evidence-based clinical guidelines for the management of thyrotoxicosis that

would be useful to generalist and subspeciality. According to common perception, hypothyroidism is held responsible for obesity. However, linking them causally is controversial. Overt hypothyroidism is associated with modest weight gain, but there is a lack of clarity regarding subclinical hypothyroidism. Novel view indicates that changes in thyroid-stimulating hormone (TSH) could well be secondary to obesity. The increasing prevalence of obesity further confounds definition of normal TSH range in population studies. Thyroid autoantibody status may help in establishing the diagnosis of subclinical hypothyroidism in obesity.

Key Words –Hyperthyroidism , Hypothyroidism , Thyroid Hormone

INTRODUCTION

Obesity and hypothyroidism are two common clinical conditions that have been linked together closely. The link has become more relevant in the context of an unprecedented rise in the prevalence of obesity worldwide. Obesity is generally regarded by patients as being secondary to thyroid dysfunction. Novel view indicates that changes in thyroid-stimulating hormone (TSH) could well be secondary to obesity. Recent data have also disclosed a relation between obesity and thyroid autoimmunity with the adipocyte hormone leptin appearing to be the key factor linking these two conditions. In this article, we will review the intriguing relationship between obesity and hypothyroidism and the consequent clinical implications.

Epidemiology of Hypothyroidism

Hypothyroidism, the condition in which the thyroid gland does not produce enough hormone, occurs in approximately 4.6% of the population in the United States.[4] The vast majority of cases involve women (85%).[1,3] Thyroid deficiency compromises almost all body functions, and if left undiagnosed or untreated, it can lead to infertility, Hashimoto encephalopathy, and myxedema coma.[3,5-7]

Autoimmune dysfunction is one of the major causes of thyroid disease.[8] In the case of hypothyroidism, Hashimoto thyroiditis is the most common autoimmune presentation. It is characterized by infiltration of the thyroid by T and B lymphocytes.[8] This leads to thyroiditis, an inflammatory reaction of the thyroid gland that leads to the production of antibodies to thyroid

antigens, thyroid peroxidase, and thyroglobulin. Ultimately, the follicular cells of the thyroid are destroyed, thereby interfering with thyroid hormone synthesis.[8]

Risk factors for developing Hashimoto thyroiditis include iodine consumption, smoking, radiation exposure, female sex, aging, and genetics.[8] Those with autoimmune thyroid disease are more likely to have other autoimmune disorders (polyautoimmunity). Polyautoimmunity is so common that guidelines now recommend searching for other autoimmune disorders in patients with autoimmune thyroid disease, as well as poor treatment outcomes, before initiating combination therapy for hypothyroidism.[8]

Clinical presentation and complications

Signs and symptoms due to excess thyroid hormones

Excess thyroid hormone affects many different organ systems. Commonly reported symptoms are palpitations, fatigue, tremor, anxiety, disturbed sleep, weight loss, heat intolerance, sweating, and polydipsia. Frequent physical findings are tachycardia, tremor of the extremities, and weight loss.

The manifestation of hypothyroidism can vary markedly from patient to patient. At this time, no clear guidelines exist for screening for hypothyroidism. The US Preventive Services Task Force does not recommend screening patients for thyroid dysfunction.[9] Other associations, including the American Academy of Family Physicians and the American College of Physicians, suggest screening for thyroid dysfunction only in women older than 60 years.[10] Some clinicians may find it reasonable to screen all patients at risk for hypothyroidism.

Treatment / Management

Treatment of hyperthyroidism depends on the underlying etiology and can be divided into symptomatic and definitive therapy. The symptoms of hyperthyroidism, such as palpitations, anxiety, and tremor, can be controlled with a beta-adrenergic antagonist such as atenolol. Calcium channel blockers, such as verapamil, can be used as second-line therapy for patients who are beta-blocker intolerant or have contraindications to beta-blocker treatment.

This review will only discuss the treatment for the most common causes of hyperthyroidism: Graves disease, toxic multinodulargoiter, and toxic adenoma in non-pregnant patients.

Indications for treatment:

1. Overt hyperthyroidism
2. Subclinical hyperthyroidism with TSH <0.1 and age >65 years
3. Subclinical hyperthyroidism with TSH <0.1 and age <65 years with comorbidities (cardiovascular disease, osteoporosis, or symptomatic)
4. Subclinical hyperthyroidism with TSH <0.1 and age <65 years, if TSH still elevated after 3 to 6 months
5. Subclinical hyperthyroidism with TSH between 0.1-0.4 and age >65 years, if TSH still elevated after 3 to 6 months
6. Subclinical hyperthyroidism with TSH between 0.1-0.4 and age <65 years with comorbidities (cardiovascular disease, osteoporosis, or symptomatic), if TSH still elevated after 3-6 months
7. Antithyroid Drugs (ATDs)

8. Thionamide drugs include methimazole, carbimazole (precursor of methimazole), and propylthiouracil. These drugs are competitive inhibitors of the thyroid peroxidase (TPO) enzyme, resulting in their ability to block thyroid hormone synthesis. Additionally, these drugs may have additional immunosuppressive effects, as shown by their ability to induce remission in patients with Graves disease. Methimazole and propylthiouracil both inhibit thyroid hormone synthesis by thyroid peroxidase. Thyroid peroxidase is the enzyme responsible for converting dietary iodine into iodide.

9. Doses:

    ATA (Americal Thyroid Association) guidelines provide a rough guide for the initial dose of methimazole based on free T4 levels

Free T4 1-1.5 times upper limit of normal: Start methimazole 5-10 mg daily

Free T4 1.5-2.0 times the upper limit of normal: Start methimazole 10-20 mg daily

Free T4 2.0-3.0 times the upper limit of normal: Start methimazole 30-40 mg daily

10. Radioactive Iodine (RAI)

11. RAI (using I-131 isotope) can be the preferred therapy in most patients, especially the ones with high-risk comorbidities who are at high risk for surgery and need definitive management. Patients who have contraindications for the use of thionamides should also undergo RAI. This procedure should be avoided in patients planning a pregnancy in the six months due to the risk of inducing hypothyroidism in the fetus. RAI is also contraindicated in lactating women. Patients will a history of moderate to severe Graves orbitopathy should not undergo treatment with RAI due to the risk of worsening eye disease. Patients with underlying thyroid malignancies should not undergo RAI.

12. Graves Disease

    A single fixed dose of 10-15 mCi (370-555 MBq) is sufficient to render a patient with GD hypothyroid. Doses of RAI can be calculated using the size of the thyroid gland and the uptake of RAI.

13. Toxic Adenoma

    A single fixed of 10-20 mCi (370-740 MBq) is usually sufficient. The dose can also be calculated based on nodule size: 150-200 microCi (5.5-7.5 MBq).Long-term studies have shown that the risk of hypothyroidism after RAI for TA is 8% in 1 year and 60% in 20 years.

14. Surgery

15. Preferred in women planning a pregnancy in less than six months, presence of active Graves orbitopathy, patients who experience significant adverse effects with the use of thionamides, when thyroid malignancy is suspected, presence of large compressive goiters, and the presence of co-existing hyperparathyroidism needing surgery. The surgical option should be avoided in patients with significant comorbidities deemed high-risk for undergoing surgery.

Future research

Treatment of hyperthyroidism has not changed greatly in the past several decades. Choices are between long-term therapy, with risk of relapse, or destruction of the thyroid gland with subsequent hypothyroidism. ATDs are a conservative option, but have about a 50% relapse rate; however, thyroidectomy and radioactive iodine treatment are definitive therapies, but with

subsequent hypothyroidism needing lifelong therapy with thyroid hormone replacement. Future research should be directed towards a better understanding of the pathogenesis of Graves' hyperthyroidism to direct therapy at the underlying cause of the hyperthyroidism and to obtain a cure that is safe, conservative, and definitive.

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