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Review Article

Guidelined Review: Management of Hypothyroidism

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INTRODUCTION

Hypothyroidism is a condition in which the thyroid gland does not make enough thyroid hormone. This condition is often called underactive thyroid.

The diagnosis and management of hypothyroidism have evolved significantly over the years, with advancements in diagnostic tools and therapeutic options. This literature review covers the overview of the current knowledge surrounding the diagnosis, classification, and management of hypothyroidism.

EPIDEMIOLOGY AND AETIOLOGY

Iodine deficiency is the leading cause of hypothyroidism worldwide, however in iodine-sufficient countries, autoimmune diseases such as Hashimoto's thyroiditis are the primary aetiology. Other causes include thyroidectomy, radiation therapy, medications (e.g., lithium), and rare genetic disorders.

Hypothyroidism affects approximately 4.74% of the patients cared for by PHCC **[1,2].** A review article notes that the prevalence of overt hypothyroidism in Europe varies between 0.2–5.3%, depending on the definition of hypothyroidism used [BMJ Best Practice, 2024]

The British Thyroid Association (BTA) advises that subclinical hypothyroidism affects 5–10% of the population [Okosieme, 2015]. The prevalence increases in women and with increasing age [Biondi, 2019].

In areas where dietary iodine is adequate, such as the UK, the prevalence of spontaneous hypothyroidism is 1–2%. It is up to 10 times more common in women than in men and increases with age [Mendes, 2019; Gottwald-Hostalek, 2022].

The prevalence of subclinical hypothyroidism is about 4 to 8.5% and may be as high as 20 percent in women older than 60 years [3].

Apart from primary gland failure other causes include Central hypothyroidism, medication induced (lithium, amiodarone, interferon -alfa, tyrosine kinase inhibitors), transient hypothyroidism (pregnancy induced hypothyroidism, postpartum thyroiditis silent and subacute thyroiditis) and iatrogenic (hyperthyroid treatment, radiation therapy and thyroid surgery).

DIAGNOSIS

- **Clinical presentation**

  Consider hypothyroidism in patients presenting with cold intolerance, lethargy, constipation, dry skin, oedema, hair changes (dry coarse hair, hair thinning or loss), change in voice, weight gain, arthralgias, difficulty focusing, memory issues, menorrhagia and infertility.

  Signs include bradycardia, coarse facial features, slow tendon reflexes, diastolic hypertension, oedema, goitre, hypothermia, lateral eye brow thinning, macroglossia, hoarseness of voice, cognitive impairment. Electrocardiography may show low voltage, pericardia effusion, periorbital oedema, pericardial effusion and pleural effusion are some of the findings

- Investigations include thyroid function tests, complete blood count (CBC), anti-thyroid peroxidase. [4]

Classification of hypothyroidism

Hypothyroidism can be classified according to:

- The time of the onset
  - Congenital
  - Acquired [5]
- Level of endocrine dysfunction as
  - Primary hypothyroidism – abnormality in thyroid gland itself
  - Secondary hypothyroidism – secondary to pituitary or hypothalamic disorder [5,6]
- Severity
  - Overt hypothyroidism
  - Subclinical [6]

Thyroid function test interpretation

Overt Primary Hypothyroidism

TSH high, Free T4 low [6,7], commence patient on Levothyroxine (after excluding transient thyroiditis).

- The aim is to restore TSH and free T4 to within reference range and symptomatic improvement, although symptomatic improvement can take some time. [7]
- A full replacement dose of Levothyroxine for adults (1.6 µg/kg daily) should be started since titration of the dose upward from a low starting dose is unnecessary for most patients. [6,7]
- Dose should be adjusted to maintain the level of thyroid stimulating hormone within the lower half of the reference range, around 0.4 to 2.5 mU/l. If the patient feels perfectly well with a level in the upper half of the reference range, then adjustment is unnecessary [7]. When TSH is low, the daily dosage should be decreased by 12.5 to 25 mcg. When TSH is high, the daily dosage is increased by 12.5 to 25 mcg per day every 6-8 weeks until TSH is normalized.
- Consider starting levothyroxine at a dosage of 25–50 micrograms per day with titration for adults aged 65 years and over and adults with a history of cardiovascular disease. [7]

Monitoring

- When levothyroxine dose is changed, a period of 6-8 weeks should elapse before re-testing (unless elderly, IHD).
- When a patient is stabilized on levothyroxine, only an annual check using TSH alone is required.
- If the TSH level is abnormal, assess patient adherence, any drug-drug interactions, and adjust the levothyroxine dosage every six to eight weeks until the TSH level normalizes.
- TSH target in patients with a history of thyroid cancer is to be suppressed to < 0.1 mU/Lin in moderate to high-risk patients. [6,7]

Medication and Levothyroxine therapy:

- Levothyroxine should be taken once per day, 30 to 60 minutes before eating, and four hours before or after drugs that may impede absorption. Proton pump inhibitors, antacids, ferrous sulfate, simethicone, calcium carbonate, orlistat and bile acid sequestrants [3].
- During pregnancy thyroxine requirements may increase by up to 50%; thyroid function tests are undertaken each trimester. During the first trimester, higher circulating human chorionic gonadotrophin (hCG) causes lowering of TSH levels, and more reliance should be placed on maintaining T4 at the upper end of the normal range [8]
- Persistently abnormal serum TSH level during levothyroxine treatment may be seen in [7]:
  - levothyroxine is taken only on the day of the blood test - thyroid function test will typically show raised TSH level but normal or raised free thyroxine levels
  - Situation where absorption of levothyroxine can be an issue e.g. - by certain medications, or malabsorption (excluding Helicobacter pylori gastritis, giardiasis, inflammatory bowel disease coeliac disease and autoimmune gastritis)
- Changing levothyroxine brands might affect TSH, earlier TSH check might be necessary.

SUBCLINICAL HYPOTHYROIDISM

Free T4 normal; TSH high. Many cases of sub-clinical hypothyroidism are transient. It is essential to confirm that abnormalities in TSH are persistent or progressive.

- Studies suggest that the average patient will not get any clinical benefit from T4 therapy until TSH rises above approximately 10mU/L. [9]
- Repeat TSH/FT4 at 3 months to exclude a transient rise in TSH. [9]
- Request anti-TPO abs to help determine if an autoimmune process is present and help predict the risk of progression to overt hypothyroidism. Patients with a higher TSH value and those with positive for thyroid peroxidase antibody (TPOAb) are more likely to progress to overt hypothyroidism [10]
- On repeat, If TSH > 10 mU/L – start treatment with levothyroxine.
- On repeat, if TSH lies between 4.0 - 10 mU/L, annual monitoring is required.
- Commence Levothyroxine when TSH subsequently becomes >10 mU/L and in a few patients, e.g., if they are symptomatic with goiter or planning pregnancy, and TPO antibodies +ve.

MYXOEDEMA COMA [11]:

Myxoedema is infrequent but serious complication of severe hypothyroidism. Often, the

condition is precipitated by exposure to cold, usually in poorly heated houses, infection or sedative drugs e.g. phenothiazines, narcotics, anaesthetics. Hypothermia is present in 80% of cases and predominantly observed in elderly individuals with primary hypothyroidism, resulting in a mortality rate ranging from 25% to 60%. Clinical manifestations apart form hypothermia includes alterations in mental status (such as lethargy, confusion, psychosis), hypotension, bradycardia, hypoventilation, and widespread nonpitting oedema. Abnormal laboratory findings consist of hypoglycaemia, hyponatremia, elevated TSH, markedly low FT4, and reduced cortisol levels in the presence of concurrent adrenal insufficiency.

REFERRAL TO SECONDARY CARE: [11]

Refer patient to emergency department if suspecting myxoedema coma or thyroid storm suspected Urgent referral to Endocrinology if difficulty in achieving euthyroid state, have another endocrine disorder, structural changes in the thyroid gland.

CONCLUSION

Hypothyroidism is common presentation in primary care, it's important to accurately diagnosis and to determine when to initiate treatment and when to just monitor the condition. Patient education is important regarding nature of the condition, compliance to medication adherence, and correct administration of levothryroxine.

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