JPSIM Journal of Pakistan Society of Internal Medicine

Medical Guidelines

Diagnosis, Monitoring and Management of Primary Hypothyroidism

Aziz-ur-Rehman
Professor of Medicine, Rashid Latif Medical College, Lahore

Thyroxine is essential for the normal function of almost all body cells. Hypothyroidism is a clinical condition resulting from inadequate level of thyroxin in the body. This is mostly due to some disease of thyroid gland itself and hence called primary hypothyroidism. In less than 5 % of the cases the problem may be in the pituitary gland or hypothalamus. These guidelines will address primary hypothyroidism only. The document is the summary of Guidelines issued by American College of Clinical Endocrinology (ACCE), American Thyroid Association (ATA) and National Institute of Care and Excellence (NICE). In our part of the world, chronic iodine deficiency is said to be the commonest cause of hypothyroidism followed by autoimmune Hashimoto's thyroiditis. Other causes include post-thyroidectomy, post-radioactive iodine ablation, over treatment with antithyroid drugs and hereditary enzymatic defects. Whatever the cause of hypothyroidism may be, the diagnostic criteria and the treatment plan is the same.

Diagnosis of Hypothyroidism:

Although hypothyroidism is often clinically suspected, yet blood test is necessary to confirm the diagnosis. Sample of blood can be taken during any part of the day and irrespective of the meal. Both, free thyroxine (FT4) and thyroid stimulating hormone (TSH) should be done for a definitive diagnosis. If clinical suspicion is low, later may suffice, as a normal TSH practically rules out primary hypothyroidism. In a typical case, FT4 is low and TSH is significantly raised. As TSH is overly sensitive test, a value of 20 or above is expected in clinically evident cases of hypothyroidism such as myxoedema. In such situations a borderline high TSH would suggest an alternate diagnosis. Thyroid peroxidase antibodies (TPOAbs) test is not necessary in all patients, but if positive, will suggest autoimmune etiology. Other tests that can be helpful but not done routinely is radioactive iodine uptake (RAIU). If done, will show reduced uptake of radiotracer. Primary hypothyroidism can be differentiated from the secondary, as TSH is low or at least not high in the later. Fig 1.

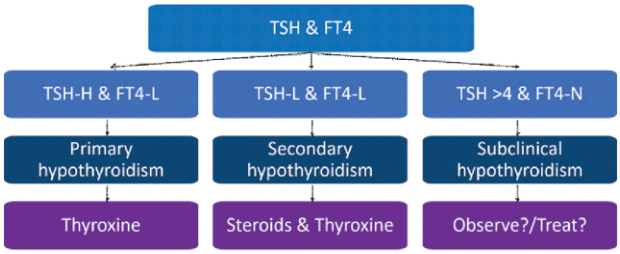

Figure 1: *If TSH is high and FT4 is low, the Diagnosis of Primary Hypothyroidism is Established, and Thyroxine may be started. If both TSH and FT4 are low, diagnosis of secondary hypothyroidism is likely. Further testing is recommended, and treatment must include corticosteroids. If TSH is above the reference range but FT4 is within the normal range, a diagnosis of subclinical hypothyroidism is made.*

Treatment of Primary Hypothyroidisms:

The drug of choice for the treatment of primary hypothyroidism is synthetic levothyroxine. There is no proven advantage of levothyroxine-liothyronine combination or thyroid extract. The starting dose of 50 mcg once daily given in the morning or at night is appropriate for most. To ensure reliable absorption and steady plasma levels, it is desired that medicine is taken on empty stomach and nothing is eaten for at least one hour afterwards. Thyroxine has remarkable tolerability; the only side effects may be related to overdosing. After 2 weeks, the dosage may be increased to 100 mcg and continued for indefinite period. TSH with or without FT4 should be done approximately 12 weeks after patient is taking estimated euthyroid dose i.e., 100 mcg. Being a protein, TSH has long half-life and will not be expected to become normal despite euthyroid dose until approximately 12 weeks. If done too early, the test will not reflect the true thyroid status and can be misleading. If necessary, further increment of 25 mcg a day can be done. Once TSH and FT4 are both in the reference range on two consecutive occasions, 12 weeks apart, the same dosage may be continued for indefinite time usually for life. Once a year monitoring is adequate as thyroxine level does not change much if patient is taking medicines as prescribed. The best quality of life

(QoL) is expected when TSH falls in the lower half and FT4 fall in the upper half of reference range. Further increments in the dosage may be necessary during acute stress situations like trauma, pregnancy, or infections.

In individuals above 65 and those where ischaemic heart disease exists or is likely, it may be safer to start with 25 mcg daily with slower increments following the principal 'start low-go slow'. In addition, the final euthyroid dose in this situation may be when TSH falls in the upper half and FT4 falls in the lower half of reference range. Fig 2.

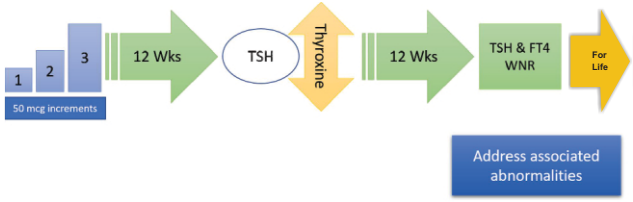

Figure 2: *The schema of starting and escalating levothyroxine for most adults. Once a euthyroid dose is achieved, the same may be continued for life. A 'start low and go slow' policy may be safer in elderly and those with ischaemic heart disease (IHD). Starting dose and increments of 25 mcg is recommended.*

Subclinical Hypothyroidism:

If the FT4 falls within the reference range (with or without symptoms) but TSH is above the reference range, the condition is described as subclinical hypothyroidism. Clinical practice guidelines are less clear in this situation and the management plan must be individualized. Table 1.

Summary Points

1. Levothyroxine is the first line treatment for all patients with primary hypothyroidism.
2. Liothyronine (T3) is not recommended as monotherapy or in combination with levothyroxine in routine.
3. For people younger than 65 and without ischaemic heart disease, starting dose of levothyroxine may be 50 mcg daily and escalated to 100 mcg daily in 2 weeks.
4. Total dose of thyroxine should be taken as once daily with water and on an empty stomach. Patient should be instructed not to take any food or other medicines for one hour afterwards.
5. For monitoring purposes, TSH and FT4 may be done every 12 weeks. Once 2 consecutive tests, 12 weeks apart, fall within the reference range, the same may be continued for indefinite period.
6. Once euthyroidism is achieved, further monitoring may be done once a year or only when symptoms warrant.
7. Further increment may be necessary during severe stress and trauma.
8. Once started, thyroxine should be continued for life for majority of the patients. For a small percentage of patients, it may be possible to withdraw thyroxine, but it should be done under medical supervision. If TSH start rising during tapering off process, the original dose should be resumed and continued indefinitely.
9. For patients with subclinical hypothyroidism wait and see policy is acceptable for majority. Thyroxine can be prescribed to those who have TSH>10, TPOAbs +ve, infertility, have heart disease or have symptoms compatible with hypothyroidism.
10. In patients with hypothyroidism and pregnancy, thyroxine is safe and essential for the fetal wellbeing. Monthly monitoring and trimester specific TSH goals should be used.

Table 1: *Management Plan for Patients with Subclinical Hypothyroidism and Conditions where Treatment with Thyroxine may be Indicated as against Wait and See*

Wait and see policy	Early treatment with thyroxine
Asymptomatic patients with incidental laboratory diagnosis of subclinical hypothyroidism and TSH < 10	Symptomatic patients (trial) TSH > 10 TPOAbs +ve Infertility Heart disease Thyroidectomy Radioactive iodine ablation

Table 2: *Desired TSH values in different Trimesters*

Trimester	Desired TSH
First	<2.5
Second	<3.0
Third	<3.5

Source

1. Managing primary hypothyroidism; Tests for people with confirmed primary hypothyroidism. https://www.nice.org.uk/guidance/ng145/chapter/recommendations#managing-primary-hypothyroidism
2. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and The American Thyroid Association. http://content.guidelinecentral.com/guideline/get/pdf/3295