Subclinical Hyperthyroidism

Disclaimer

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Background

About Subclinical Hyperthyroidism

- Subclinical hyperthyroidism is defined biochemically by a serum TSH concentration below lower limit of normal (0.1 to 0.4 mIU/L) but normal serum FT4 and FT3 concentrations.
- Typically patients have few or no symptoms of hyperthyroidism.
- Most common causes are treatment with thyroxine, and autonomously functioning thyroid nodules and multinodular goitres.
- Subclinical Graves' disease and painless thyroiditis are less common causes.

- Thyroiditis
  - The most common cause of thyroiditis is sub-acute (de Quervain's) thyroiditis.
  - Subacute thyroiditis (also known as de Quervain’s)
    - Where there is a tender diffuse goitre with transient hyperthyroidism followed by hypothyroidism before the restoration of normal thyroid function. It is presumed to be caused by a viral infection or post-viral inflammatory process.
    - Beta blockers and non-steroidal anti-inflammatory drugs may be used for symptom control.
  - May also be painless.
  - This is a destructive process.
  - Patients with subacute or painless thyroiditis do not respond to carbimazole.
  - Other causes of thyroiditis include postpartum thyroiditis (painless), medications (amiodarone, lithium, interferon, immunomodulatory drugs in cancer), and external radiation.

- Graves' disease
  - An Autoimmune disease.
  - Most common cause of hyperthyroidism (about 70%).
  - 10 times more common in women.
  - Usually associated with diffuse goitre.
  - May have associated ophthalmopathy (20 to 40%).
  - 10% do not have positive standard thyroid antibodies (TSH receptor antibodies).

- It is worth noting that in patients with thyroid cancer, subclinical hyperthyroidism is the goal of thyroid hormone therapy, to suppress thyroid cancer growth. The benefits of TSH suppression are thought to outweigh the risks of subclinical hyperthyroidism in these patients.
- Increases risk of developing atrial fibrillation and osteoporosis, especially if TSH is fully suppressed.
- Affects 6% of people aged > 55 years.
- 50% of cases resolve within 1 year without treatment.
- 1 to 4% develop overt hyperthyroidism per year.
Assessment

1. Establish whether the patient is pregnant or breastfeeding.
2. Ask the patient about health food shop iodine supplements e.g., kelp tablets.
3. Consider the fracture risk and risk of atrial fibrillation (AF) in relation to age, sex, BMI, smoking status, alcohol intake, hypertension.

Management

1. Stop any iodine supplementation, including health food shop iodine supplements e.g., kelp tablets.
2. Repeat TFTs in 3 to 6 months.
3. Monitor pregnant patients.

Transient subclinical hyperthyroidism in pregnancy

- Also called hCG or BhCG-mediated hyperthyroidism, as hCG has a weak thyroid stimulating effect.
- Occurs when hCG levels are highest in the first trimester, peaking at 10 to 12 weeks.
- Transient subclinical hyperthyroidism occurs in 10 to 20% of normal pregnant women, and does not require treatment.
- Check for symptoms or signs of hyperthyroidism, otherwise monitor in the second trimester with blood tests every 4 to 6 weeks.
- If there is doubt about the diagnosis, refer or discuss with an obstetrician or an endocrinologist.

4. If breastfeeding, monitor every 4 to 6 weeks and consider routine endocrinology referral.

5. For TSH persistently (> 12 months) ≤ 0.1 to 0.4 mIU/L, consider risk for developing AF or low bone density.
   - If low risk for AF or fracture, monitor TSH 6 to 12 monthly and assess risk factors yearly.
   - If high risk for AF or fracture, arrange radionuclide thyroid scan and bone density scan.
   - If low bone density, increased cardiovascular risk, or increased uptake on thyroid scan, start low dose carbimazole and arrange routine endocrinology referral.

Carbimazole dose

- Subclinical (normal FT4 and FT3): 2.5 to 5 mg daily.
- Mild (FT4 or FT3 < twice the upper limit of normal): 5 to 10 mg daily.
- Moderate (FT4 or FT3 > twice the upper limit of normal): 10 mg twice a day.
- Severe (FT4 or FT3 > 3 times the upper limit of normal) or with marked symptoms (tachycardia, rapid weight loss): 15 mg twice a day plus a beta blocker.

Warnings about carbimazole

- Warn all patients about the sudden, serious complication of agranulocytosis.
  
  Agranulocytosis risk
  - Advise patients to stop taking carbimazole and seek medical attention straight away if they develop symptoms of infection e.g., fever, flu-like symptoms, sore throat, mouth ulcers.
Arrange urgent FBE so that results are available on the same day. If neutrophil count is low, arrange immediate endocrine surgery referral or admission.

The incidence of agranulocytosis resulting from carbimazole therapy is reported to be between 0.2% (1 in 500) to 0.5% (1 in 200).

➢ Document informed consent about the risks of agranulocytosis and hepatotoxicity.
➢ Take baseline FBE and LFTs before starting carbimazole.

**Baseline FBE and LFTs before starting carbimazole**

Mild neutropenia or mild liver function derangement are often seen as a result of hyperthyroidism, and should normalise as thyroid hormone levels return to normal.

Consider adding a beta blocker for initial control of marked symptoms (tachycardia, palpitations, tremor, etc.).

➢ Hepatitis rarely occurs with carbimazole so routine monitoring of LFTs is not recommended.
➢ Other less serious adverse effects are rashes, arthralgia, and gastritis.
➢ Routine FBEs are not recommended.

Note: Suggest documentation of informed consent about the risks of agranulocytosis and hepatotoxicity.

6. For TSH persistently (> 12 months) < 0.1 mIU/L, arrange radionuclide thyroid scan and arrange routine endocrinology referral.

### Referral

If available, include the results of thyroid function tests and relevant imaging in all referrals.

- If patient is pregnant and there is doubt about the diagnosis, arrange urgent endocrinology referral or discuss with an endocrinologist.
- Arrange routine endocrinology referral:
  - for all patients with hyperthyroidism.
  - if patient started on carbimazole.
  - if low bone density, increased cardiovascular risk, or increased uptake on thyroid scan, or discuss with an endocrinologist.
  - if TSH persistently (> 12 months) < 0.1 mIU/L.
- If breastfeeding, consider routine endocrinology referral.
- If you are unsure about management options, phone or fax an endocrinologist for advice.

### Information

#### For patients

➢ Better Health Channel:
Patient:
- Overactive Thyroid Gland: Hyperthyroidism
- Thyroid Function Tests

**Sources**

Select bibliography


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