Hyperthyroidism

Lead Author
Riaz I

Co-Authors
Bhanu K Bhakhri, Shalmi Mehta

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Remesh Kumar R
IAP President 2022

Upendra Kinjawadekar
IAP President-Elect 2022

Piyush Gupta
IAP President 2021

Vineet Saxena
IAP HSG 2022–2023
IAP Standard Treatment Guidelines Committee

Chairperson
Remesh Kumar R

IAP Coordinator
Vineet Saxena

National Coordinators
SS Kamath, Vinod H Ratageri

Member Secretaries
Krishna Mohan R, Vishnu Mohan PT

Members
Santanu Deb, Surender Singh Bisht, Prashant Kariya, Narmada Ashok, Pawan Kalyan
Hyperthyroidism

Introduction

- **Hyperthyroidism**: Production and secretion of excess amounts of thyroid hormone from the thyroid gland.
- **Thyrotoxicosis**: The hypermetabolic clinical syndrome which occurs when there are elevated serum levels of T3 and/or T4.

Epidemiology

- Hyperthyroidism accounts for 10–15% of thyroid disorders in children.
- Age at presentation—it is less common in children <5 years. Peak incidence is at 10–15 years.
- It is more common in girls.
Hyperthyroidism

**Flowchart 1:** Etiology of hyperthyroidism.

Graves’ disease accounts for >95% cases of hyperthyroidism.
- It is an autoimmune condition and is caused by a complex interaction of genetic, environmental, and immune factors.
- Thyrotropin receptor antibodies (TRAb) stimulate thyroid-stimulating hormone (TSH) receptor and increased thyroid hormone production and release.
- A family history of autoimmune thyroid disease may be present.

The most common clinical features of hyperthyroidism among children are:
- Weight loss
- Palpitations
- Anterior neck swelling

While older children also commonly present with sleep disturbance, poor scholastic performance, and easy fatigability. Increased stool frequency may be seen commonly in younger children.

Other symptoms are excessive sweating, tremors, hair loss, and headache.

The features of ophthalmopathy like lid retraction, scleral injection, and proptosis are reportedly less commonly noticed among children.
To establish hyperthyroidism—mechanism.

**Fig. 1:** Mechanism of hyperthyroidism.

<table>
<thead>
<tr>
<th>TSH</th>
<th>Suppressed</th>
</tr>
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<tbody>
<tr>
<td>FT4/FT3</td>
<td>Raised</td>
</tr>
</tbody>
</table>

To find out the causes of hyperthyroidism

- **Thyrotropin receptor antibody:**
  - It usually raised in Graves’ disease.
  - It also helps in predicting the risk of relapse after stopping antithyroid drugs.
- **Technitium-99m scan for thyroid gland:** It shows increased uptake in Graves’ disease. This can help differentiate between Graves’ disease and Hashimoto’s thyroiditis (in early stages, due to release of preformed thyroid hormones, there could be hyperthyroidism; however, there is decreased uptake on the thyroid scan) (**Fig. 2**).

**Fig. 2:** Technitium-99m scan.
(SSN: superior salivatory nucleus)
Hyperthyroidism

Investigations

- Ultrasonography
  - Usually diffuse enlargement of the gland is visible
  - Increased vascularity
  - Helps in ruling out solitary nodule/multinodular goiter.

- Complete blood count (CBC)
- Liver function test (to be done before starting antithyroid drugs)
- Fine-needle aspiration cytology (FNAC): This is required only if malignancy is suspected during the evaluation of diffuse goiter or thyroid nodules.

Other Investigations

- Complete blood count (CBC)
- Liver function test (to be done before starting antithyroid drugs)
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Treatment

- The initial goal of therapy is the control of symptoms and normalization of biochemical parameters.
- Definitive therapy is considered among children who fail to produce early and long-standing remission.

Flowchart 2: Algorithm for the management of hyperthyroidism.

- Clinical and laboratory evidence of hyperthyroidism
  - Start beta blockers for symptomatic relief
  - Diffuse goiter
    - Antithyroid drugs with close monitoring
      - Remission achieved over 1–2 years of therapy
        - Yes
          - Taper, titrate and stop treatment
        - No
          - Definitive therapy surgery or Radioiodine ablation (preferred among adolescents)
  - Nodular goiter

- Antithyroid drugs with close monitoring
  - Remission achieved over 1–2 years of therapy
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The preferred initial therapy for children with variety of etiological causes is antithyroid drugs (ATDs).

Methimazole (MMI) 0.1–1 mg/kg/d or carbimazole 0.5–0.7 mg/kg/d is preferred over propylthiouracil (PTU) among children.

The relevant details of each treatment option are provided in Table 1.

<table>
<thead>
<tr>
<th>Therapeutic option</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithyroid drugs</td>
<td>Patient preferred</td>
<td>Risk of adverse effects</td>
<td>The chances of achieving remission gradually increase with prolonged therapy</td>
</tr>
<tr>
<td></td>
<td>Effective initial control</td>
<td>Limited chances of complete remission</td>
<td></td>
</tr>
<tr>
<td>Radioiodine ablation (RIA)</td>
<td>Option for patients trying to avoid surgery</td>
<td>Takes several weeks to achieve remission</td>
<td>Require lifelong monitoring and replacement for hypothyroidism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not recommended for children &lt;5 years of age and not preferred for children 5–10 years of age</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of relapse. Long-term suspected risk of developing malignancy (not supported with literature)</td>
<td></td>
</tr>
<tr>
<td>Surgery (total or subtotal thyroidectomy)</td>
<td>Immediate results</td>
<td>Risk of developing hypoparathyroidism</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Preferred among children with nodular goiter</td>
<td>Experienced surgeons are recommended for good results</td>
<td></td>
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</tbody>
</table>

The dose of ATD is titrated with the goal to achieve free T4 and T3 estimation within normal range. Addition of beta-blockers like propranolol, 1–2 mg/kg/d helps in early control of symptoms and their dose can be titrated based upon the reported symptoms.

If remission is not achieved, ATD can be safely continued over 1–2 years of duration after which the definitive therapy, either in form of radioiodine ablation (RIA) or surgery, should be considered. Surgery and RIA are preferred over ATD among hyperthyroid children with toxic nodule or multinodular goiter.
Hyperthyroidism

Monitoring and Follow-up

- Free T4 and T3 should be estimated every 4–6 weeks for the initial titration of ATD doses.
- Once the euthyroidism is achieved, 3 monthly monitoring is optimal.
- The baseline CBCs and liver functions should be checked before the initiation of ATD.
- Children should be clinically monitored for potential adverse effects of ATD which are urticarial rash, agranulocytosis, hepatic dysfunction, arthralgia, and other vasculitis associated symptoms which may warrant repeat laboratory testing.
- If surgery is chosen as definitive therapy, the calcium and parathyroid hormone (PTH) levels should be closely monitored during and after the perioperative period for timely supplementation with calcium and calcitriol.
- After RIA or thyroidectomy, the thyroid status should be monitored with free T4 and TSH levels for guiding the replacement doses.

Outcome

- Some children with milder presentation of Hashitoxicosis show good symptom control over short therapy with only beta-blockers medications. Others may require few months of ATD before achieving complete remission which is usually permanent.
- Almost one-third children with Graves’ disease achieve complete remission after initial ATD trial and there is a considerable risk of relapse once the ATD is stopped. Hence, families should be provided the options for definitive therapy early in the course of disease.
- After RIA or thyroidectomy, children need lifelong hormonal replacement for hypo-thyroidism.