

# Treatment of thyrotoxicosis

## Lecture 2

**Prof. Ahmed Shaaban**

**Professor of Pharmacology &  
Senior Consultant of Endocrinology**



# TREATMENT OF THYROTOXICOSIS

## 1. Thiarnides (thioarnides, thiourea)

### Mechanism

1. Competitive inhibition of thyroperoxidase (by Cu chelation) causing inhibition of the 2nd, 3rd and 4th steps of iodine cycle.
2. ↓TRABs (TSH RAB); TSI & TGI → immunosuppression.

### Uses

1. Hyperthyroidism (Graves disease and toxic nodular goiter) for 1-2 years. In 50% of cases relapse occurs after years and requires continued treatment.

ttt of subclinical hyperthyroidism ↓ mortality, cardiac diseases & fractures.

2. Before subtotal thyroidectomy by 1-2 months to ↓T4 synthesis.



## Adverse effects

Dose & pt. – dependent. Serum sickness manifestations (1-7).

1. Agranulocytosis : most dangerous . More in older pts., higher doses, usually within 1st 3 months ttt onset.

Sudden onset. Sore throat, fever, malaise, manifestations of inflammation, → CBC (↓neutrophils). May be rapidly fatal.

Stopping ... resolves within a week.

ttt by broad spectrum bactericidal antimicrobials & granulocyte colony - stimulating factors.

No switching to another thionamide (50% cross sensitivity).



2. Skin rash : most common

3. Hepatotoxicity: Severe hepatocellular by propyl thiouracil. May be fatal. Carbimazole may cause cholestatic jaundice.

4. Fever.

5. Nausea and vomiting.

6. Lymphadenopathy.

7. Joint pain.

8. Goiter :  $\downarrow T4 \ \& \ T3 \rightarrow \uparrow TSH$ .

9. Fetal goiter: They cross placenta to fetus causing suppression of thyroid gland, increasing TSH  $\rightarrow$  enlarged fetal thyroid  $\rightarrow$  obstruction of delivery.

10. Excretion in milk.

Switching from one preparation to the other  $\rightarrow$  similar in 50% of cases.



# Preparations

1. **Carbimazole** or (also →) methimazole. Potent, delayed onset (4-6 weeks after T4 depletion) & long duration

Used in thyrotoxicosis. Tablets 5 mg, initial dose in severe cases 30-60mg /day (6-12 tablets) in divided doses for 6 weeks till reaching euthyroid state, then 1-2 years titration regimen with maintenance dose 5 -15 mg /day.

2. **Propyl thiouracil** or methyl thiouracil. The dose is 10 times that of carbimazole with rapid onset. More toxic.

It inhibits T4 to T3 conversion (used in thyrotoxic crisis).

It crosses placenta less than carbimazole due to more plasma protein binding (used in pregnancy in smallest dose possible).



## Iodides. 2 •

### Mechanism

They antagonize TSH action on protease enzyme, decreasing release of T4 causing  $\uparrow$  colloid in acini  $\rightarrow$  compression  $\rightarrow$   $\downarrow$  size and vascularity of the gland.

### Uses

1. Before thyroidectomy by 1-2 weeks to  $\downarrow$  size & vascularity of thyroid gland.
2. Thyrotoxic crisis.



## Disadvantages & precautions

1. Short duration (escape phenomenon).

Used only for short term therapy.

2. ↑ intraglandular T4 causing delay of onset of thiamide action.

3. Delay use of radioactive iodine for several weeks.

4. Allergy, rhinitis, fever & iodism.

5. Not in pregnancy (crosses placenta → goiter).

6. Not alone for ttt.

## Preparations

Lugol's iodine: 5% I<sub>2</sub> + 10% KI (8mg /drop) .



# $\beta$ blockers .3 •

## Mechanism

1. Block peripheral & central adrenergic effects in hyperthyroidism, decreasing HR, tremors, anxiety & sweating.
2. Inhibit peripheral outer mono deiodination of T4 into T3 → inner monodeiodination → rT3 (inactive).

Inadequate control (does not affect I2 cycle), so alone may cause crisis

## Uses

1. Thyrotoxic crisis.
2. + KI preoperative and continue 5 days after operation.

## Dose

$\beta$  blockers without ISA e.g. propranolol (lipophilic, with central action), 40mg tds and 1mg IV (in crisis) have good action but for short period.

If  $\beta$  blockers are contraindicated Ca ch. blockers diltiazem or verapamil are used.





# Radioactive iodine I<sub>131</sub>I •

## Mechanism

1. Emission of  $\beta$  irradiation  $\rightarrow$  local ionization  $\rightarrow$  tissue damage and fibrosis (for treatment).
2.  $\gamma$  - irradiation for diagnosis (diagnostic dose is 5 microcurie).

## Uses

1. Investigation of thyroid function.
2. Thyrotoxicosis in old pts . and recurrence after medical & surgical treatment.
3. Cancer thyroid.
4. Multinodular goiter.



## Disadvantages

1. Slow onset of action.
2. Hypothyroidism.
3. Radiation thyroiditis.
4. Contraindicated in pregnant & lactating females and children.

## Advantages

(onset 2 weeks and peak 3 months)

1. For outpatients treatment and cheap.
2. No surgical risk, scar or injury to parathyroid gland or recurrent laryngeal nerve.
3. Once controlled → permanent cure.

**Dose** (therapeutic): 5 m curie.



# Thyrotoxic crisis (storm)

By: ↓ ttt, stress, surgery, infection and sudden stop of antithyroid drugs.

## A) Curative

1. Propyl thiouracl.
  2. Propranolol.
  3. Corticosteroids.
  4. Iodides.
  5. Lithium.
- 1-3: ↓T4-T3 conversion.  
3-5: ↓T4 & T3 release.
- 6.L- carnitine: ↓T4 & T3 passage into nucleus.
  7. Plasmapheresis: removes thyroid Abs.

## B) Symptomatic

1. Cooling blankets
2. Fluids .
3. Antipyretics
4. Sedatives.

