

Thyroid hormones 2023

I. Hormones - physiology

1. TSH

- stimulates thyroid cell growth and differentiation
- stimulates iodine uptake and organification
- releases T₃ and T₄ from Tg

2. Thyroid hormones – T₃ and T₄

- T₃ more bioactive than T₄
- most T₄ is converted to T₃, which has a high affinity for the peripheral nuclear thyroid hormone receptor (TR)
- thyroid hormone receptor modulates various genes expression

3. Effects of thyroid hormones:

- liver - fatty acid β -oxidation and gluconeogenesis
- lipolysis
- heart - \uparrow heart rate
- pituitary gland - suppress production of hypothalamic TRH and pituitary TSH
- muscle – sensitization to insulin

II. Drugs used in the management of hypothyroidism

Levothyroxine

Levothyroxine+ liothyronine

Indications:

- replacement for hypothyroidism
- prevention of goiter recurrence after resection
- prevention of thyroid cancer recurrence (not anaplastic)

Relative contraindications:

- angina, MI
- myocarditis
- arrhythmias

Interactions:

- Ion exchange resins limit absorption
- thyroxine \uparrow action of hydroxycoumarin derivatives
- thyroxine \downarrow effect of antidiabetic agents

Side effects:

- no side effects with correct dosage
- overdosage \rightarrow symptoms of hyperthyroidism (cardiology) + hyperglcaemia
- Long-term administration in high doses in non-deficient patients – osteoporosis

III. Drugs used in the management of hyperthyroidism

1. Thioamide derivatives:

- thio-urea derivatives: propylthiouracyl

- thioimidazole derivative: thiamazole (methimazole)

By acting as a substrate for the catalyst thyroid peroxidase, inhibit the incorporation of iodide into the thyroid hormone precursor, thyroglobulin. Consequently, the drugs are iodinated and

degraded within the thyroid gland. Oxidized iodine is diverted away from thyroglobulin, which effectively diminishes the biosynthesis of thyroid hormone. Inhibit iodothyrosine coupling to iodothyronine.

Thio-urea derivatives block peripheral conversion additionally !

T₁ / 2 for imidazole depends on the concentration of the drug in the gland and its effect is longer than its half-life. These data do not apply to thiourea.

Indications:

- hyperthyroidism
- preparation for surgery
- preparation for radioactive iodine therapy

NOTE – iodine and iodine-containing drugs (including shading agents) reduce the thyrostatic effect.

Adverse effects:

- skin allergy, taste disturbance, hair loss, transient leukopenia (1 – 5%)
- liver damage
- agranulocytosis (0,2 – 0,5%)
- aplastic anemia, thrombocytopenia, vasculitis (<0,2%)
- iatrogenic hypothyroidism, thyroid enlargement, worsening of ophtalmopathy

Contraindications

- severe liver damage
- severe hematological diseases
- retrosternal goiter (risk of pressure on the trachea)

Thyreostatic use in pregnant women

- their use is avoided
- if necessary in the first trimester - propylthiouracyl
- after the first trimester –thiamazole

2. Radioactive iodine – ¹³¹I (RIT)

Mechanism of action:

- radioactive iodine is uptaken by hyperactive thyroid cells and incorporated into thyroglobulin molecules (sodium iodide symporter NIS, hNIS) - it causes cell death
- early discomfort in the neck, worsening of hyperthyroidism (immediately after administration) and temporary increase in: anti-TPO, anti-Tg, anti-TSH-R
- worsening of ophtalmopathy (smokers! steroids after RIT, eg. prednisone 30 mg)
- very rarely radiation sickness (redness and pain in the neck)
- at very high concentrations > 1000mCi (progression of thyroid cancer?, leukemia, gonadal damage) – generally low risk

Age:

- In middle-aged and older
- during procreation (in the first phase of menstrual cycle, pregnancy tests must be performed before treatment in all women of reproductive age)
- children (intolerance to thyreostatics, hyperthyroidism in the course of other diseases e.g. Down Syndrome)

Indications:

Mild thyroid disease

- hyperactive nodular goiter
- Graves' disease

- autonomic adenoma
- giant goiter - in the absence of the patient's consent to a strumectomy

Thyroid cancers

- follicular
- papillary
- anaplastic (rarely)
- medullary – resistant to ^{131}I

Contraindications

- pregnancy (necessity to postpone pregnancy for 6-12 months after radioiodine therapy)
- lactation
- absence of the patient's consent

3. Lithium carbonate

- Ionised lithium inhibits thyroglobulin proteolysis which inhibits the release of thyroid hormones into the blood stream resulting in a prolonged biological half-life of iodine
- Inhibits conversion of T4 to T3
- reduces level of thyroid hormones transporting proteins in plasma

these effects have led to the use of lithium carbonate as an adjunct treatment for both hyperthyroidism and thyroid cancer

4. Perchlorates, e.g. sodium perchlorate (NaClO_4), potassium perchlorate

Mechanism of action: competitive antagonism in iodide uptake by the thyroid gland

Indications:

- before examination with an iodine-containing contrast agent in patients at risk of thyrotoxic crisis (perchlorates are then used with thiouracil derivatives)
- amiodarone-induced hyperthyroidism

Adverse effects:

- gastrointestinal disorders
- agranulocytosis, aplastic anemia
- nephritic syndrome

Contraindications:

- pregnancy, lactation

5. Other agents

Beta-receptor blocking agents

Mechanism of action:

- blockade of beta receptors, reduction of symptoms of the hyperthyroidism in the cardiovascular system
- propranolol inhibits peripheral conversion of T4 to T3.

Glucocorticoids

- inhibit peripheral conversion of T4 to T3
- used to treat thyrotoxic crisis and after RIT in Graves' disease

IV. Thyroid crisis (thyroid storm) – management

1. Inhibition of thyroid hormone synthesis – thyreostatics (preferred thiourea derivatives due to inhibition of peripheral conversion at a dose of 200-250 mg every 4h)
2. Inhibition of thyroid hormone secretion - iodine or lithium carbonate (iodine supply should be preceded by 1 - 2 hours using a high dose of thyrostatics)
3. Inhibition of peripheral conversion: organic iodine, corticoids, beta blockers, and propylthiouracil
4. Blocking β -adrenoreceptors
5. Correction of metabolic disorders and organ failure
6. Removal of excess thyroid hormones: plasmapheresis, dialysis or fresh plasma transfusion

V. Drugs affecting thyroid dysfunction:

- amiodarone
- alpha interferon
- iodine - contrast agents - jopainic acid
- lithium carbonate
- NSAIDs
- tricyclic p-depressants, neuroleptics