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AN OVERVIEW ON "SYMPTOMS, DIAGONOSIS OF THYROID DISORDER AND DRUG TREATMENT FOR THYROID DISORDER"

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ABSTRACT

Thyroid hormones are produced by the thyroid gland. Examples of thyroid hormones are triiodothryonine T_3 and thyroxine T_4. They are used for regulation of metabolism. Iodine is necessary or essential for the production of T_3 and T_4. Decreases the level or production of T_3 and T_4, it gives enlargement of thyroid tissue and it will gives or cause disease like goiter. These hormones are commonly found in the blood. Thyroxine T_4 was commonly found in the blood. In human body, this hormone was released into the blood in ration 20:1. Thyroxine T_4 was converted into triiodothryonine T_3within the cell by deiodinases i.e. 5'-iodinase. Triiodothryonine T_3 is more potent than thyroxine T_4. Triiodothryonine T_3 is converted into iodothyronamine i.e. T_1a and thyronamine i.e. T_0a by decarboxylation and deiodination processes. Dietary selenium is essential for T_3 production. T3 is also known as Liothyronine in the pharmaceutical industries.Iodide was actively absorbed from the blood stream by the process known as iodide trapping. In this process, sodium ion i.e. Na was co-transported with iodide from the basolateral side of the membrane into the cell and then concentrated in the thyroid follicles to about thirty times its concentration in the blood. When two molecules of diiodotyrosine are react with each other then it give thyroxine i.e. T4. When one molecules of MIT and one molecules of DIT react with each other, it gives triiodothryonine i.e. T3.

KEYWORDS

Thyroid hormones, Triiodothryonine i.e. T_3, Thyroxine i.e. T_4, MIT and DIT.

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INTRODUCTION

Thyroid hormones are essential for every cell in the body. It increases the basal metabolic rate. They act on the protein synthesis. They help to regulate long bone growth and neutral maturation. Thyroid hormones are used to increase the body's sensitivity to catecholamine like adrenaline. Thyroid hormones are essential for good or proper development and

differentiation of all cell of the human body. They are used to regulate protein, fat and carbohydrate metabolism. They give stimulation for vitamin metabolism. Thyroid hormones are used for heat generation in human. They are used to inhibit neuronal activity. (Figure No.1 Thyroid system).

Function of T3 and T4

The primary function of thyroid gland is production of thyroid hormone like T3 and T4 and calcitonin. It gives approximately 80% of T4 is converted into the T3 by human organs like liver, kidney and spleen. T3 is more potent and more powerful than T4.

Synthesis of thyroid hormones was produced from individual thyroid follicular cell. Thyroglobulin is produced from endoplasmic reticulum and it gives secretion pathway that enters the colloid in the lumen of the thyroid follicle by exocytosis. Sodium-iodide (Na/I) pumps iodide (I^-). Iodide (I^-) can easily enter into human cell. Thyroglobulin and iodide (I^-) combine with each other, it gives complex that crossed the endothelium by unknown mechanism. Iodide (I^-) enters into follicular lumen from cytoplasm by pendrin transporter. Oxidation of iodide (I^-) is converted into iodine (I^0) by enzyme thyroid peroxidase. Iodine (I^0) is very reactive. Complex re-enter into the follicular cell by endocytosis. Thyroxine T4 was synthesized by follicular cells from free tyrosine and by tyrosine residue of the protein known as thyroglobulin i.e.TG. Iodine was captured with the iodine trap by the hydrogen peroxide which is generated by enzyme thyroid peroxidase i.e. TGO. Iodine react with or link to the 3' and 5' sites of the benzene ring of the tyrosine residues on TG, and on free tyrosine. When stimulation of follicular cell by thyroid stimulating hormone i.e. TSH, follicular cell reabsorbs thyroglobulin i.e. TG and cleave the iodinated tyrosine from liposome's, it gives T_4 and T_3. Thyroid gland gives production of T_4 and T_3. Approximately 80-90 % of T_4 was produced and 10-20% of T_3 was produced. T_4 was converted into T_3 by deiodinases enzymes. They give effect on the cells of the developing brain. Thyroid hormone is essential for brain maturation during fetal development. T_4 can easily cross the blood brain barrier i.e. BBB. T3 can also cross the brain cell membrane by second transport protein i.e. MCT 8. T3 can also activate phosphotidylinositol 3-kinase. T_4 and T_3 are partially bound to thyroxine binding globulin i.e. TBG, transthyretin and albumin in blood. Only small amount of these hormones are unbound i.e. 0.03% T_4 and 0.3% T_3. Effect of this thyroid hormone on human body was carried out by free fraction thyroid hormone. Thyroid hormone can easily cross the cell membrane and bind to the intracellular receptors likeα_1, α_2, β_1 and β_2 and combine with retinoid X-receptor as transcription factors to modulate DNA transcription.

T_3 and T_4 regulation

The production of thyroxine and triiodothyronine was regulated by thyroid stimulating hormone i.e. TSH. They are released from anterior pituitary gland. TSH production was suppressed when the T_4 levels are high. The TSH production itself is modulated by thyrotropin releasing hormone like TRH. Thyrotropin releasing hormone like TRH was released or produced by the hypothalamus and secreted at an increased rate in situations such as cold exposure. Thyroid stimulating hormone i.e. TSH production is blunted by somatostatin i.e. SRIH and released by glucocorticoids and sex hormones like estrogens and testosterone and give high blood iodide concentration. An additional hormone was produced by the thyroid contributes to the regulation of blood calcium levels, parafollicular cells produces calcitonin.

Effect of triiodothyronine

In thyroid hormones, the effect of triiodothyronine T3 is commonly present in active form. They give following biological effects likes,

Increases the cardiac output.
Increases heart rate
Increases the ventilation rate
Increases the basal metabolic rate
Increases the effect of catecholamine i.e. increases the sympathetic activity
For brain development
To increases the endometrial size.
Increase metabolism of proteins and carbohydrates.

Uses

- Both T_3 and T_4 are used to treat thyroid hormone deficiency i.e. Hypothyroidism. They are both absorbed well by the gut, so can be given orally.
- Levothyroxine is used in the treatment of hypothyroidism. It contain T4 hormone and it metabolized into T3. They give slow metabolism than T3. Dose of this drug is once in day.
- Some natural thyroid hormones are developed from or derived from the pig thyroid glands. It is used in the treatment of hypothyroid disorder. It contains about 20 % T3 and some amount of T_1 and calcitonin.
- In market, some synthetic combination of thyroid hormones is available like T_3/T_4 in different ratios like Liotrix and pure T3 thyroid hormone containing Liothyronine.
- They are used to controlled hypothermia. This hypothermia occurs in the brain.
- They are used in the treatment and preventing damage during ischemic shock.
- Synthetic thyroxine was discovered or introduced by the scientist Charles Robert Harington and George Barger in 1926.

Formulation

Currently, most of the patient was treated with levothyroxine or any similar synthetic thyroid hormone. Currently now also natural thyroid hormone supplement are also available in the market. Natural thyroid hormone supplements are made by from the dried thyroids of animals. Levothyroxine contains only T4 so that they are ineffective for the patient who unable to convert T4 to T3. These patients may choose to take natural thyroid hormone as it contains a mixture of T4 and T3 or any alternative supplement. Currently, some natural thyroid hormone brands are F.D.A. approved, but some are not. Thyroid hormones are well tolerated. Thyroid hormones or thyroid supplements are usually not dangerous for pregnant women or nursing mothers, but should be given under or as per prescription given by doctors. If a woman who is hypothyroid is left untreated, her baby is at a higher risk for birth defects. When pregnant, a woman with a low functioning thyroid will also need to increase her dosage of thyroid hormone. In treatment, one exception is that thyroid hormones may aggravate heart conditions, especially in older patients.

Thyroid disorder

Thyroid disorder or thyroid diseases are as follows,
Hyperthyroidism i.e. abnormal increased activity
Hypothyroidism i.e. abnormal decreased activity
Thyroiditis i.e. inflammation of the thyroid
Thyroid nodules i.e. benign thyroid neoplasm or tumours that lead to thyroid cancer.
All these Thyroid disorder or diseases can also gives rise to a goiter i.e. enlargement of thyroid gland.

Hyperthyroidism

Hyperthyroidism or increased activity of thyroid is defined as an over production of thyroid hormones like T3 and T4. They commonly give or cause Graves's diseases. This disease is an example of autoimmune diseases. In this disease, an antibody was stimulated by thyroid gland. This gland secretes excessive amount or quantities of thyroid hormone. This disease gives formation or production of a toxic goiter. Goiter gives negative feedback mechanisms. It gives symptoms like thyroid goiter, protruding eyes, palpitation, excessive sweating, diarrhoea, weight loss, muscles weakness and increases the body heat.

Beta blockers are commonly used in the treatment of hyperthyroidism. It decreases the symptoms of hyperthyroidism like increased the heart rate, tremors, anxiety and heart palpitations. Beta blockers are commonly used with combination like beta blocker and anti thyroidal drug. These combinations are used to decrease production of thyroid hormones. This combination is also used in the treatment of Graves's diseases. Dose of this combination was taken for several months to gives full effect. It also gives some side effects like skin rash and decreases the white blood cell count. Dose can be prescribed by doctors and it includes one pill for every hours. For the treatment of goiter diseases,

blood test may useful. Due to presences of side effect, some patient can be treated by radioactive iodine-131. Radioactive iodine-131 can destroy a portion of or the entire thyroid gland since the radioactive iodine is selectively taken up by the gland and gradually destroys the cells of the gland. Alternative method for this disease is partially or entirely removes the gland by surgery.

Hypothyroidism

Hypothyroidism means decreases the production of thyroid hormone i.e. T3 and T4. Hypothyroidism disorder gives following disorders,

Congenital thyroid abnormalities i.e. Thyroid deficiency at birth

Autoimmune disorders such as Hashimoto's Thyroiditis.

Iodine deficiency.

Symptoms of Hypothyroidism

Some symptoms are commonly observed in hypothyroidism like weight gain tiredness, baldness, cold intolerance and bradycardia. The thyroid is unable to produce T_3 and T_4 and as a result, the thyroid may continue to grow to form a non-toxic goiter. It does not produce toxic quantities of thyroid hormones. For the treatment of hypothyroidism, hormone replacement therapy like levothyroxine drug was commonly used. It gives negative feedback mechanism that gives growth of thyroid hormone.

Anti thyroidal drug classification

Anti thyroidal drug is example of hormone antagonist drugs. They are acts on the thyroid hormones. They includes following drugs like,

- Carbimazole
- Methimazole
- Propyl thiouracil
- Potassium prechlorate
- Goitrin

Carbimazole is available in the United Kingdom, Methimazole is used in United State and Propyl thiouracil is available in both United Kingdom and United State. Potassium prechlorate is commonly used in the market. These anti-thyroidal drugs are used in the treatment of Graves's diseases. For this disease, they are used for six month to two years. Single dose/day of Methimazole is effective for treatment of Graves's diseases for 12 weeks.

Carbimazole

Carbimazole is an example of anti thyroidal drug. This drug is used in the treatment of hyperthyroidism. This drug is example of pro drug. After absorption, Carbimazole drug is converted into the active metabolite like Methimazole. This drug inhibits and prevents the thyroid peroxidase enzyme. This enzyme is essential for the coupling and iodination the tyrosine. Tyrosine is converted into the thyroglobulin. It gives result in reduction of thyroid hormones like T3 and T4. Carbimazole drug can easily cross the placenta so that in pregnancy period, this drug is used. Carbimazole drug is available in the form of brand name like Neomercazole and Vidalta.

Uses

- This drug is used in the treatment of hyperthyroidism.
- Dose of this drug is starting from 15 mg to 40 mg and it continued until the patient has normal thyroid function and then dose will be reduced up to 5-15mg.

Side effect

Common side effect of this drug is rashes and pruritus. These side effects of this drug can be treated with anti histaminic drug without stopping the Carbimazole. When patient was sensitive then alternative drug was used i.e. propyl thiouracil. Rare side effect of this drug is bone marrow suppression i.e. neutropenia and agranulocytosis. Other common symptoms or side effect is sore throat and fever.

Methimazole

Methimazole is also known as Tapazole and thiamazole or MMI. This drug is an example of anti thyroid drug. This drug is class of thioamide group. It gives common side effects like agranulocytosis. This drug is active metabolite of Carbimazole.

Uses

- Methimazole is used in the treatment of hyperthyroidism. Hyperthyroidism is occurs when the thyroid gland secrete or produces excesses amount of thyroid hormone.

- This drug may take before thyroid surgery and this drug is used for decreasing the thyroid hormone levels.
- This drug is used in the treatment of hyperthyroidism in cats. This drug is used as veterinary drug.

Mechanism of action

Methimazole inhibit the enzyme thyroperoxidase enzyme. The enzyme thyroperoxidase is essential for thyroid synthesis. This enzyme is used for conversion or oxidizing the action iodide (I-) to iodine (I0), this drug is used to inhibit the thyroglobulin which necessary or essential step in the synthesis of triiodothyronine i.e. T3 and thyroxine i.e. T4. This drug does not inhibit the action of sodium dependent iodide transporter which is present on follicular cells of basolateral membranes.

Drug interaction

This drug gives drug interaction with some drugs. When this drug was administered with anti coagulants like warfarin, digoxin, theophylline and vitamin then it gives side effect.

Side effect

The common side effect of this drug is agranulocytosis. Rare side effect of this drug is decreases the white blood cells count and neutropenia. Other known side effects of this drug are skin rash, itching, abnormal hair loss, abdominal pain, upset stomach, vomiting, loss of taste, abnormal sensation, swelling, joint and muscle pain; drowsiness, dizziness, decreases the white blood cells, and decreases the platelet count.

Propyl thiouracil

Propyl thiouracil is also known as 6-n-propyl thiouracil. This drug is an example of thiouracil drug. This drug is used in the treatment of hyperthyroidism. This drug is used to treat Graves's diseases. It decreases the production of thyroid hormone from thyroid gland. Common side effect of this drug is agranulocytosis and aplastic anaemia. This drug was approved for the treatment of hyperthyroidism diseases on 3rd June 1947. This drug was approved by United State of Food and Drug Administration in 1947.

Mechanism of action

Propyl thiouracil inhibits the enzyme thyroperoxidase. This enzyme is essential for the thyroid hormone synthesis. This enzyme helps for conversion of iodide to iodine by oxidation. This drug inhibit the thyroglobulin which is essential for production of thyroxine i.e. T4. This drug does not inhibit the action of sodium dependent iodide transporter which is present on follicular cells of basolateral membranes. This drug also gives action or acts by inhibition of the enzyme 5'-deiodinase i.e. tetraiodothyronine 5'deiodinase. This enzyme is used in conversion of T4 into T3.

Pharmacokinetic

This drug can be administered by oral administration. Peak plasma or serum concentration was achieved within the 1 hour. Approximately 70% drug bound to the protein. The plasma half life of this drug is 1 hours. Dose interval for this drug is 8 hours. Less than 10% drug was excreted into the urine. This drug was metabolized into liver via glucuronidation or by hepatic metabolism.

Side effect

Common side effect of this drug is agranulocytosis and decreases the white blood cell count. This drug gives effect on gastrointestinal tract i.e. nausea, vomiting and abdominal pain. This drug is well tolerated and easily administered by orally. Other known side effect of this drug is skin rash, itching, abnormal hair loss, abdominal pain, upset stomach, vomiting, loss of taste, abnormal sensation, swelling, joint and muscle pain; drowsiness, dizziness, decreases the white blood cells.

Potassium prechlorate

Potassium prechlorate is an example of inorganic salt. The molecular formula of this drug is $KClO_4$. This drug is strong oxidizer. This drug reacts with organic material but very slowly. This drug is available in the form of colorless, crystalline powder. It is used in the fireworks, explosive primers and in propellant. It is used as solid rocket propellant. It gives slow solubility. It is used as anti thyroid drug. This drug is used in the treatment of hyperthyroidism. This drug is used in combination with other drug.

Goitrin

Goitrin is an example of sulfur containing oxazolidine. It is cyclic thiocarbamate drug. This drug is used to reduce the production and releases of thyroid hormone like thyroxine. This drug is found in the vegetable like cabbage and rapeseed oil. This drug can be synthesized in the laboratory by the hydrolysis of a progoitrine.

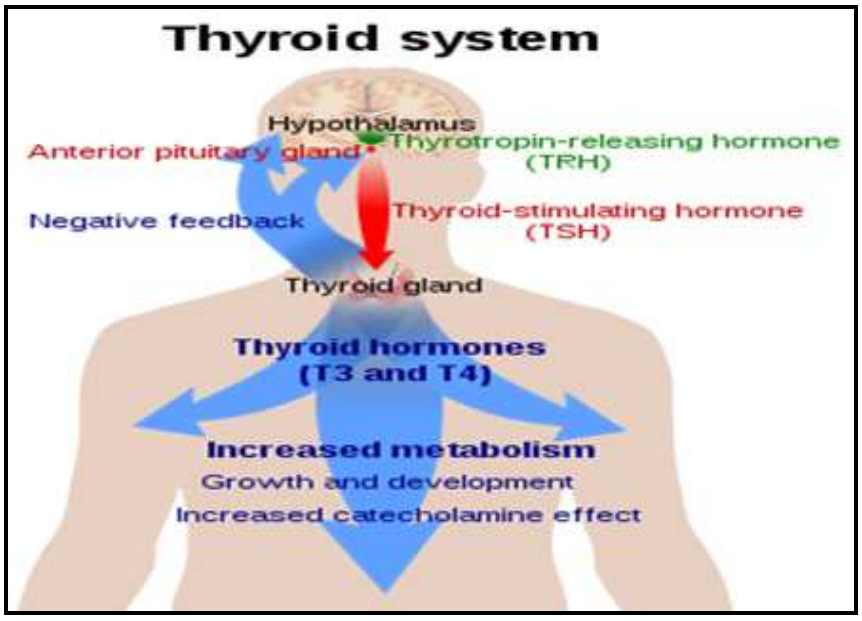
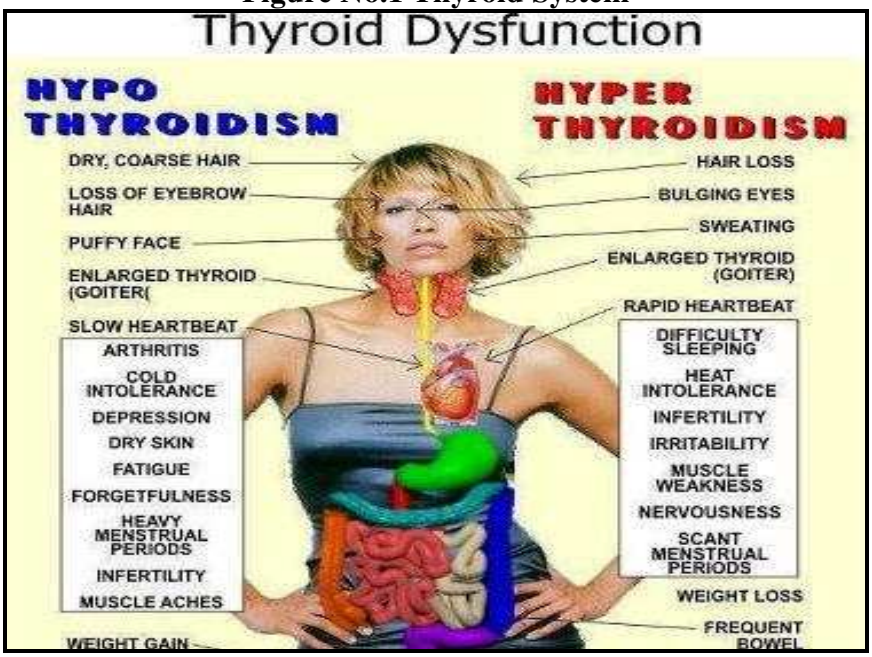
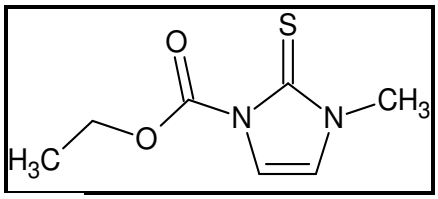


Figure No.1 Thyroid System

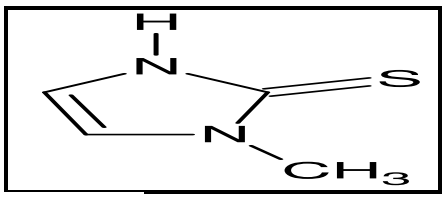


Carbimazole



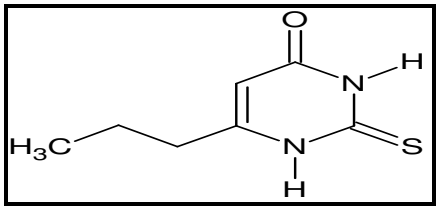
Systematic (IUPAC) name
Ethyl 3-methyl-2-sulfanylidene-imidazole-1-carboxylate

Methimazole



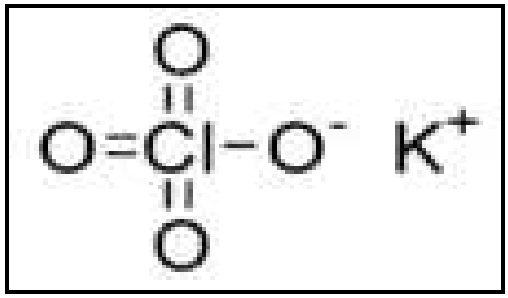
Systematic (IUPAC) name
1-methyl-3*H*-imidazole-2-thione

Propyl thiouracil

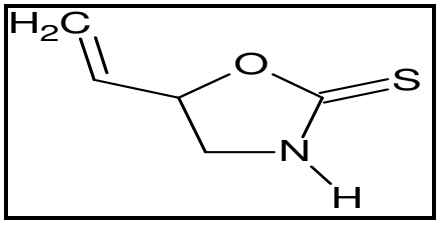


Systematic (IUPAC) name
6-propyl-2-sulfanylpyrimidin-4-one

Potassium prechlorate



Goitrin



Systematic (IUPAC) name
5-ethenyl-1, 3-oxazolidine-2-thione

CONCLUSION

Thyroid hormones are essential for good or proper development and differentiation of all cell of the human body. They are used to regulate protein, fat and carbohydrate metabolism. They give stimulation for vitamin metabolism. Thyroid hormones are used for heat generation in human. They are used to inhibit neuronal activity.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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