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Review Article

Pharmacological Survey of Graves' Disease: A Mini Review

Akhtar Saifi[1], Negar Sadat Taheri[2], Hadi Reza Mansourian[3], Azad Reza Mansourian*[4]

1. Department of Pharmacology, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran
2. Department of Obstetrics & Gynecology, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran
3. Department of Emergency, Hakim Jorjani Hospital, Gorgan, Iran
4. Metabolic Disorders Research Center, Department of Biochemistry, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran

*Correspondence: Azad Reza Mansourian, Metabolic Disorders Research Center, Department of Biochemistry, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran
Email: azad_r_mansourian@yahoo.com

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ABSTRACT

Thyroid hormones play a key role indevelopment of most metabolic disease. Toxic multi nodular goiter, toxic adenoma and thyroid autoimmunity are the most common causes of thyrotoxicosis. Graves' diseaseis an autoimmune thyroid disorder characterized by production of autoantibodies against thyroid-stimulating hormone receptor on the thyroid gland.G raves' disease-related thyrotoxicosis can be controlled either through medication or surgical and radiotherapy interventions. There are few options for the prevention of thyroid hormones overproduction including antithyroid drugs such as methimazole and propylthiouracil, carbimazole, radioactive iodine as well as thyroidectomy. In this study, the latest pharmacological information on treatment of Graves' disease are reviewed.

Keywords: Thyroid hormones; Hyperthyroidism; Graves disease; Antithyroid drugs

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INTRODUCTION

The diagnosis of hyperthyroidism relies on the thyroid function test carried out by the laboratory serum measurement of thyroxin(T4), triiodothyronine (T3) and thyroid stimulating hormones (TSH), accompanied by other laboratory examinations suggested by clinicians and endocrinologist. In thyrotoxicosis, serum level of thyroid hormones, particularly T4,is elevated, which is accompanied by pituitary TSH suppression reaching to undetectable levels in sever thyrotoxicosis. Toxic multinodular goiter, toxic adenoma and thyroid autoimmunity are the most common causes of thyrotoxicosis (1-3). The focus of this review is on Graves' disease, an autoimmune thyroid disorder that targets TSH receptor on the thyroid gland. It seems that autoimmunity is among the leading causes of hyperthyroidism in humans (4). As one of the main classes of hyperthyroidism, Graves' disease is characterized by the production of TSH receptor-stimulating antibodies, leading to thyrotoxicosis. Although the exact cause of this autoimmune abnormality is not clear, it is widely understood that genetic, environmental andnutritional factors, such as iodine intakecan influence the incidence of this disease. Graves' disease-related thyrotoxicosis can be controlled through either medication to disrupt the biosynthesis of thyroid hormones or by surgical and radiotherapy intervention (4-11).

Therapeutic regiments in hyperthyroidism (Graves' disease)

There are few options to prevent the overproduction of thyroid hormones including antithyroid medications (methimazole, propylthiouracil and carbimazole), radioactive iodine therapy as well as thyroidectomy. Medication is the preferable option to avoid the adverse outcomes of aggressive treatment such as radioactive iodine, radiation therapy and invasive thyroid operation for either partial or total thyroidectomy (12-14). On the other hand, antithyroid agents seem to be unable to solve the patient problems indefinitely and disease recurrence is reported in patients with hyperthyroidism following consumption of these drugs. This recurrence might be related to different factors including drugs guidelines as well as patient's clinical and genetic characteristics (15,16-18).

Due to the autoimmune nature of Graves' disease, immune suppressive medications such as corticosteroid and non-corticosteroids are prescribed for the patients. In this regard, some investigators suggested administration of complementary dosage of immune suppressive agents or levothyroxin for TSH suppression with subsequent reduction of thyroid antibodies in order to prevent the recurrence of Graves' disease (19-21). Methimazole is often preferred to propylthiouracil in treating hyperthyroidism, but there is no significant difference in disease recurrence following medication discontinuation (21-23). Rash and hepatic complications are common side effects of these drugs accompanied with agranulocytosis and liver damage due to drug poisoning. Investigation showed that methimazole exhibits longer half-life with fewer adverse effects. It should be noted that therapeutic procedures are prohibited during the first trimester of pregnancy (11,13,24).

Anti-thyroid drugs dosage wildly depends on the clinical condition of patients, although the initial duration of methimazole therapy was up to six months, recent findings indicate that about 1-1.5 years of methimazole therapy could prevent the recurrence of disease. In addition, a dose of 20-40 mg/day is recommended for patients with Graves' thyrotoxicosis (25,26). The reason for biosynthesis of TSH receptor antibodies is the overproduction of TSH; therefore, levothyroxine therapy is suggested to lower serum level of TSH. However, the efficacy of this medication in Graves' disease is controversial. The concurrent administration of immune suppressive medications along with antithyroid drugs can significantly lower the risk of recurrent in patients with Graves' disease. However, the adverse effects of immunosuppressive medications on metabolism, bones, muscles and leukocyte should be taken into account (27-32).

The incidence of Graves' disease and its recurrence are significantly higher among the younger population, particularly females under forty years of age. It has been reported that the higher serum estrogen level in females may be related to higher titer of TSH autoantibodies among this population (14, 33-37). Although the incidence of Graves' disease is higher among females, the risk of disease recurrence following treatment cession is higher in male patients, which can be due to the physiological and

biochemical differences between males and females (38-40). The free T3/free T4 ratio is an important indicator of disease recurrence after medication discontinuation (13, 41-43). The measurement of serum TSH, which is released through the pituitary gland and controls thyroid hormone production should be evaluated routinely in the management of Graves' disease (14- 15).

The recurrence of Graves' disease is accompanied with anatomical enlargement of the thyroid gland leading to toxic thyroid with catastrophic side effects (14,38).

Eye vision disorder is one of the complications of Graves' disease. The clinical presentation may vary from very mild to severe irreversible vision-threatening complications (40). Genetic and environmental factors that affect the onset and recurrence of Graves' disease should also be considered when managing the disease (41-47).

CONCLUSION

Graves' disease is one of the main causes of hyperthyroidism with autoimmune related pathophysiology against TSH receptor. There are different therapeutic regiments such as methimazole, propylthiouracil, carbimazole, radioactive iodine and thyroidectomy in addition to immune-suppressive medications (corticosteroid and non-corticosteroid) to fight Graves' disease in clinical practice. However, some treatments methods may be preferred depending on the advantages and disadvantages. Although the incidence of this disease is higher in females, males are at elevated risk of disease recurrences following treatment discontinuation. Choosing the best treatment regimen depends on different factors including the clinical manifestation and disease severity. Physicians should be aware that the best treatment approach could prevent disease progression and consequently avoid other aggressive treatments such as radioactive iodine, radiation therapy and invasive thyroidectomy.

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Ethics approvals and consent to participate

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Conflicts of interest

There are no conflicts of interest to declare

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