

Expert Opinion

MANAGEMENT OF HYPERTHYROIDISM IN MALAYSIA AND THE CONTEMPORARY ROLE OF RADIOIODINE THERAPY – A REVIEW

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ABSTRACT

Hyperthyroidism is one of the commonly encountered endocrine disorders. Strategies in the management of hyperthyroidism have been well documented including the role of radioiodine therapy. This review article highlights the management and treatment options of hyperthyroidism especially in Malaysia and discusses the contemporary utilisation of radioiodine therapy emphasising on the fixed dose regimen.

Keywords: hyperthyroidism, management, radioiodine

Introduction

Thyroid glands that consist of follicles have the ability to concentrate iodide from the ingested dietary iodine in order to produce thyroid hormones. Thyroid hormones cause significant effects on our metabolism and growth. Thyroid hormones in the form of thyroxine (T₄) are transported to peripheral tissues before being converted to more metabolically active tri-iodothyronine (T₃). Thyroid stimulating hormone (TSH) plays an important role in regulating the function of the thyroid glands. Benign disorders of the thyroid glands may present with alteration in the thyroid function accompanied by goitre or thyroid lesions.

Management of hyperthyroidism

The state of excessive thyroid hormones or thyrotoxicosis is caused by various aetiologies such as Graves' disease, thyroiditis, factitious thyroxine intake and struma ovarii while hyperthyroidism is commonly relates to a hyper-functioning thyroid gland. Nonetheless, the terms hyperthyroidism and thyrotoxicosis are interchangeably used¹. So far, there is no official statistic available on the prevalence of hyperthyroidism in Malaysia. Whereas in the United Kingdom, prevalence of hyperthyroidism among women is 2% while among men is 0.2%¹. Graves' disease, toxic multinodular goitre (MNG) and toxic adenoma are among the most commonly encountered causes of hyperthyroidism^{2,3}.

Among the symptoms thyrotoxicosis are excessive sweating, hand tremors, anxiety, irritability, palpitation and weight loss in spite of good appetite. Patients may also present with any of the associated complications such as hypokalaemic periodic paralysis, pretibial myxedema, thyroid cardiomyopathy and ophthalmopathy⁴. Institutional studies in Malaysia showed the prevalence of thyroid associated ophthalmopathy among Graves' disease patients was approximately 34.7%⁵, while hypokalaemic periodic paralysis were present in 5.0% of the cases⁶.

Confirmatory diagnosis of hyperthyroidism is usually done by laboratory measurement of the serum TSH and free T₄. In fact the diagnostic accuracy improves when both parameters are evaluated particularly when hyperthyroidism is strongly suspected³. Measuring free T₄ is preferred compared to total T₄ as measurement of total T₄ is affected by protein binding abnormalities⁴. However, in patients with low TSH but normal free T₄ such as in early stage of the disease or autonomously functioning thyroid nodule, only the serum T₃ level may be elevated and hence should be measured³.

Additional laboratory test to detect thyroid receptor antibodies is particularly useful in diagnosing Graves' disease as it is a sensitive marker of the disease. Other relevant investigations that would be helpful are the radioiodine uptake study and radionuclide thyroid scan^{3,4}. Ultrasonography of the thyroid gland is also occasionally being performed as part of the disease assessment. Thyroid ultrasound remains a valuable tool in the estimation of thyroid volume and characterisation of

palpable nodules as well as in sonographic guided fine needle aspiration biopsy⁷.

Generally, treatment options for hyperthyroidism consist of anti-thyroid drugs, surgery and radioiodine therapy. In Malaysia, majority of patients are treated with thionamide anti-thyroid drugs up to 18-24 months before being tapered off. Hong et al.⁸ described that the most consumed thionamide anti-thyroid drug in Malaysia was carbimazole (82.8%) followed by propylthiouracil (17.2%). However, prolonged used of thionamides may cause minor and transient adverse effects such as skin rash, itchiness and mild leucopenia. The most dangerous side effect is agranulocytosis which can occur in approximately 0.5% of the patients⁹. As for surgery in hyperthyroidism, the indications include cases of goitre with pressure effects, suspected thyroid malignancy, severe progressive ophthalmopathy or when medical therapy fails⁴.

Role of radioiodine therapy

The oral administration of radioactive Iodine-131 (I-131) has been a well-recognised procedure for the treatment of both benign and malignant thyroid disorders since the 1940s¹⁰. Common clinical indications for radioiodine therapy of benign disorders are Grave's autoimmune disease, toxic MNG and adenoma. Absolute contraindications for I-131 therapy include pregnancy and breastfeeding¹¹. Radioiodine therapy for hyperthyroidism is used substantially more frequent in the United States compared to Europe and parts of Asia¹². The reason for I-131 therapy among patients who had received anti-thyroid drugs is mainly because of failure of medical treatment¹³.

I-131 is a beta-emitter radionuclide producing principal beta-particle with a maximum energy of 0.61 MeV and an average energy of 0.192 MeV travelling in the range of 0.4 mm in tissue^{10,11}. Thyroid gland receives the highest radiation absorbed dose. The basis radioiodine therapy is physiological whereby I-131 is taken up by iodide transporter of the thyroid and processed the same way as natural iodine. Subsequently the beta-particles will destroy the follicular cells, gradually leading to volume reduction and control of thyrotoxicosis¹⁴.

The goal of radioiodine therapy for hyperthyroidism is to achieve a non-hyperthyroid status either a euthyroid state or iatrogenic hypothyroidism¹⁰. Following I-131 treatment, hypothyroidism is defined as low free T₄ with high TSH requiring thyroxine hormone replacement, euthyroid is defined as normal thyroid function without any thyroid medication and hyperthyroidism requiring further radioiodine is defined as relapsing high free T₄ and suppressed TSH at one year post therapy^{15,16}. Around 50–90% of hyperthyroid patients are cured within one year following I-131 therapy¹⁷.

In general, therapy with I-131 for hyperthyroidism has minimal adverse effects with no significant evidence to suggest an increased risk of developing malignancy.

Transient exacerbation of hyperthyroidism symptoms due to radiation thyroiditis may occur within 1-2 weeks post therapy¹⁴. However, these symptoms usually respond to short-term beta blocker therapy if required. Thyroid ophthalmopathy may worsen or develop after I-131 therapy for Graves' disease, especially in smokers¹⁰. It has been suggested by several studies that these patients should be covered with steroids¹⁴.

Therapy with fixed dose regimen

Widely used methods for determining the dose of I-131 activity for treatment of hyperthyroidism are by prescribing (a) fixed dose regimen, (b) dose corrected for thyroid size as well as iodine uptake study and (c) quantity of I-131 calculated to deliver a specific radiation dose to the thyroid¹⁸. However, a fixed dose regimen has been suggested to be simple, more convenient and effective to achieve therapy goals^{14,16}. No advantages could be demonstrated in using adjusted or calculated dose method besides no differences in the time to outcome between the fixed and adjusted dose methods¹⁹. Jaiswal et al²⁰ reported that there was no statistically significant difference between the success rates of the two methods at 3 months post therapy among Graves' disease patients.

In Malaysia, the therapy with I-131 for thyroid diseases has become one of the main therapeutic services available at several hospitals and institutions with nuclear medicine facilities. Locally most of the nuclear medicine centres prescribe a fixed dose of radioiodine with consideration given to the thyroid size made on clinical palpation and assessment²¹. A Summary of Consensus for the Management of Thyroid Disorders in Malaysia has emphasised a fixed dose approach of 370–555 MBq (10–15 mCi) for hyperthyroidism⁴.

Similarly, latest guideline by the American Thyroid Association has recommended that sufficient radiation should be administered in a single dose, typically 370–555 MBq (10–15 mCi) to render patients with Grave's disease hypothyroid³. Lewis et al.¹⁵ reported that a single standard dose of 550 MBq (14.9 mCi) to be highly effective in treating hyperthyroidism in a study that includes Graves' disease and toxic MNG. In another study among hyperthyroidism patients in South India, good therapy outcome was seen following administration of doses less than 370 MBq (10 mCi) for normal sized thyroid glands and approximately 555 MBq (15 mCi) for large thyroid glands²².

Conclusion

As nuclear medicine services expand in Malaysia, the option of radioiodine therapy for benign thyroid disorders has become more accessible and available. Radioiodine therapy for hyperthyroidism aims to attain a non-hyperthyroid status either a euthyroid state or iatrogenic hypothyroidism requiring thyroxine replacement. In our

local setting, the widely adopted method is to administer a fixed dose regimen of radioiodine therapy as it has been recommended to be simple, more practical and effective to achieve therapy goals.

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