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## Radioactive iodine ablation therapy: a viable option in the management of graves' disease in Nigeria

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### Abstract

**Background:** Graves' disease is an autoimmune disorder characterized by hyperthyroidism and associated features. Management of this disease condition for many decades has been largely by surgical and medical intervention. Usage of anti thyroid medication ameliorates the symptoms and effects of excessive production of thyroid hormones. Recently in Nigeria, Nuclear medicine facility became available with the option radioiodine ablative therapy for the management of Graves disease. This study highlights the benefits of radioiodine therapy against the background of equally viable medical and surgical practice.

**Patients material and method** All the 36 patients seen from the inception of Nuclear Medicine facility at the University College Hospital from June 2006 to May 2010 were included in this study. Sources of referral were compiled. All the patients were on anti thyroid medication at presentation. Thyroid scan was performed by Siemens E- cam gamma camera 20 minutes after intravenous injection of 3-5mCi of Tc-99m-Perchnetate. The patients with "diffuse toxic goiter" on thyroid scan were given 10mCi of Iodine-131 orally and discharged home with radiosafety precautions. Most of the patients were treated 5 days post discontinuation of antithyroid medication. The patients were followed-up monthly with thyroid function tests to determine commencement of replacement therapy.

**Result:** Peak incidence of Graves' disease was at 6<sup>th</sup> decade (38.9%) of all patients studied. This disease was commoner in women with a ratio of 8 to 1. Ten (27.8%) patients became hypothyroid at the 3<sup>rd</sup> month post radioactive iodine -131 treatment, while the remaining 20(55.6%) patients became hypothyroid at the 5<sup>th</sup> month. Six patients were lost to follow up. There was no recurrence of hyperthyroidism in all patients treated. Twenty eight (93.3%) patients were maintained on 100mcg of levo-thyroxine daily, while 2(6.7%) patients had more than 100mcg of levo- thyroxine daily as maintenance dose.

**Conclusion:** Radioactive iodine therapy presents a safe and effective alternative to the older conventional mode of management of Graves' disease

**Keywords:** Graves' disease management, radioactive iodine ablation, iodine therapy

### Résumé

**Contexte:** La maladie de Grave (maladie de Basedow) est une maladie auto-immune caractérisée par l'hyperthyroïdie et les traits afférents. Le traitement de cette maladie pendant de nombreuses décennies a été en grande partie par intervention chirurgicale et médicale. L'utilisation de médicaments pour lutter contre la thyroïde améliore les symptômes et les effets de la production excessive d'hormones thyroïdiennes. Récemment, au Nigeria, le service de médecine nucléaire est apparu avec l'option de la thérapie ablative de l'iode radioactif pour le traitement des maladies de Graves. Cette étude met en évidence les avantages de la thérapie iode radioactif contre la pratique médicale et chirurgicale également viables.

**Matériel et méthode des patients:** Tous les 36 patients vus depuis la création du centre de médecine nucléaire du centre hospitalier universitaire d'Ibadan de Juin 2006 à mai 2010 ont été inclus dans cette étude. Les références ont été compilées. Tous les patients prenaient des médicaments contre la thyroïde lors de la présentation. La échographie thyroïdienne a été réalisée par Siemens E-cam caméra gamma 20 minutes après l'injection intraveineuse de 3-5mCi de Tc-99m-perchnétate. Les patients souffrant de «goitre toxique diffus» sur échographie pour la thyroïde ont pris 10mCi de l'iode-131 par voie orale et renvoyés à la maison avec des précautions radioprotection. La plupart des patients ont été traités 5 jours après l'arrêt du médicament contre la thyroïde. Les patients ont été suivis tous les mois avec des tests de la fonction thyroïdienne pour déterminer le début de la thérapie de remplacement.

**Résultat:** La pointe de cas de la maladie de Grave (Basedow) était à la 6<sup>e</sup> décennie (38,9%) de tous les patients étudiés. Cette maladie est plus fréquente chez les femmes avec un rapport de 8 à 1. Dix (27,8%) patients sont devenus hypothyroïdiens au 3<sup>ème</sup> mois après le traitement par l'iode radioactif -131, tandis que les 20 autres (55,6%) patients sont devenus hypothyroïdiens au 5<sup>ème</sup> mois. Six patients n'ont pas été suivis. Il n'y avait pas de récurrence de l'hyperthyroïdie chez tous les patients traités. Vingt-huit patients (93,3%) ont été maintenus à 100 mcg

de lévo-thyroxine par jour, tandis que 2 (6,7%) patients avaient plus de 100mcg de lévo-thyroxine par jour comme dose d'entretien.

**Conclusion:** Le traitement à l'iode radioactif présente une alternative sûre et efficace que l'ancienne mode classique du traitement de la maladie de Grave (Basedow)

### Introduction

Graves' disease is an autoimmune disorder characterized by hyperthyroidism, diffuse goiter, ophthalmopathy and rarely, dermopathy. It accounts for 60-80% of all cases of hyperthyroidism<sup>1</sup>. Other causes of hyperthyroidism include; nodular thyroid goiter, thyroiditis, hormone producing tumour of the pituitary gland, ovary or testes and iodine induced hyperthyroidism from iodine containing drugs. Predisposing factors for Graves' disease include; genetic susceptibility (including HLA alleles), stress, smoking, (especially associated with ophthalmopathy), female sex (sex steroids), postpartum period, iodine (including amiodarone) and lithium. Rare factors include; interferon- $\alpha$  therapy, highly active antiretroviral therapy (HAART) for HIV infection and cam- path 1-H monoclonal antibody (for multiple sclerosis) [2,3,4]

The hyperthyroidism and goiter of Graves' disease are caused by stimulation of the thyroid by TSH receptor antibodies [5]. Production of this antibody is primarily within the thyroid gland [6] and the immunology underlying this process has been described in details elsewhere [7]. It has been suggested that a genetic clonal lack of suppressor T cells may be responsible for the under regulated production of TSH receptor antibody [8].

Clinical features of Graves' disease includes features due to hyperthyroidism – heat intolerance, profuse sweating, weight loss (with hyperphagia), palpitation, hyper defecation, tremulousness and tremor. Others include oligomenorrhoea/ amenorrhoea, erectile dysfunction/gynaecomastia etc. Many manifestations of hyperthyroidism, including palpitations and tremor, are due to increased adrenergic tone [9] and may be confused with an anxiety disorder.

Elderly patients commonly present in an atypical fashion with only weight loss and anorexia or isolated atrial fibrillation [10]. Elderly patients also tend to have their symptoms for longer periods, with smaller multinodular goiters and do not have ocular signs or symptoms [11].

Graves' disease can be diagnosed clinically or biochemically. Presence of symptoms and signs of

hyperthyroidism, goiter and ocular signs and symptoms make the clinical diagnosis of Graves' to be self evident. Biochemically, Graves' disease patients' exhibit elevated free or total  $T_4$  and  $T_3$  with a low or, in most cases suppressed thyroid stimulating hormone (TSH). However, 10% of patients will have an increased total or free  $T_3$  level in the face of normal free thyroxine (FT4) and suppressed TSH level, a condition termed " $T_3$  toxicosis" [12]. Confirmation of Graves' disease by an increased 24-hour radioiodine uptake (RAIU) is recommended; because painless thyroiditis and Graves' disease have occurred at different times in the same patient [13] Measurement of levels of circulating TSH receptor antibody may eventually replace the need for the RAIU for confirmation of the diagnosis. Thyroid nodules associated with Graves' disease may have a higher likelihood of malignancy and may be more aggressive if cancerous, therefore, a thyroid scan is recommended for all patients [14]. Patients whose scan reveal a photopenic ("cold") defect should have an ultrasound guided fine-needle aspiration cytology (FNAC) to rule-out thyroid malignancy.

Management modality for Graves' disease before now in Nigeria was either surgical or medical coupled with antithyroid drugs, with attendant side effects. With the commissioning of the Department of Nuclear Medicine, University College Hospital, Ibadan in April 2006, another treatment option with radioactive iodine (RAI-131) was heralded.

The goals of treatment of Graves' disease are to efficiently control symptoms and restore euthyroidism. The most popular treatment for Graves' disease in North America by far is radioiodine [15]. This popularity reflects confidence in its overall safety and effectiveness. Concern over the potential consequences of surgery and disappointment in the high relapse rate following treatment with anti-thyroid drugs makes radioiodine treatment a welcome development.

A single dose of radioactive iodine is about 90% effective in curing of Graves' disease [16]. In the remaining 10%, second dose of radioactive iodine is needed. Radioactive iodine therapy cures hyperthyroidism by destroying the hyperthyroid cells. Radioactive iodine takes months to have its full effect, although symptoms should definitely improve after about four weeks. Short term side effects may include nausea and vomiting, painful swelling and enlargement of salivary glands. This study highlights the effectiveness of radioactive iodine treatment option in patients that hitherto would have been managed either medically or by surgical intervention.

### Patients, materials and method

All the 36 patients with clinical and biochemical features of Graves' disease seen from inception of Nuclear Medicine facility at the University College Hospital in June 2006 to May 2010 were included in this study. Sources of referral were compiled. All the patients were on antithyroid medication at presentation. Thyroid function tests (TFT) were done to determine the base line of the thyroid gland activity before radioactive iodine treatment. 3-5mCi of Te-99m-Pertechnetate was injected intravenously to each patient, 20 minutes after; thyroid scan was performed using Siemens E- cam gamma camera. Patients that had solitary "cold nodules" on thyroid scan were sent for ultrasound guided FNAC to rule-out the possibility of thyroid malignancy. The patients with "diffuse toxic goiter" on thyroid scan were given 10mCi of Iodine-131 orally. Most of the patients were treated 5 days post discontinuation of antithyroid medication. It was ensured that the female patients were not pregnant at the time of RAI treatment and were advised them not to become pregnant 6 months following treatment. Adequate instruction on radiation safety precautions to other family members were given to patients on discharge post therapy. The patients were followed-up monthly with thyroid function tests to determine commencement of replacement therapy. Patients are usually maintained on 50-150 µg levothyroxine (T<sub>4</sub>) daily

### Results

Peak incidence of Graves' disease was at 6<sup>th</sup> decade (38.9%) as shown in the Table 1. Out of the total 36 patients treated, 6 patients (17.6%) were lost to follow-up. Twenty (20 of 36) patients (55.6%) were referred from the surgical unit of this hospital, while 12 patients (33.3%) were medical referral from other hospitals in Nigeria. Four patients (11.1%) presented primarily to our department having been directed by friends who were treated earlier for the same illness.

Table 1: Showing incidence of graves' disease.

Age range	Total (%)
21-30	2(5.5%)
31-40	8(22.2%)
41-50	6(16.7%)
51-60	14(38.9%)
61-70	4(11.1%)
71-80	2(5.5%)

This disease was commoner in women with a ratio of 8 to 1. Ten (27.8%) patients became hypothyroid at 3<sup>rd</sup> month post RAI-131 treatment,

while the remaining 20(55.6%) patients became hypothyroid at the 5<sup>th</sup> month. There was no adverse reaction to radioiodine in all the patients treated. There was cessation of previous signs and symptoms of hyperthyroidism in all the patients seen.

Twenty eight (93.3%) patients were maintained on 100mcg of levo-thyroxine daily, while the remaining 2(6.7%) patients had more than 100mcg of levo- thyroxine daily.

### Discussion

Prior to the availability of radioactive iodine (RAI) therapy at the Nuclear Medicine department of University College Hospital, management of Graves' disease has been largely by medical or surgical intervention. RAI therapy is a painless procedure where the excessive production of thyroid hormone stimulated antibodies to thyroid stimulating hormone receptor is controlled

Radioactive iodine is administered orally as iodine 131 in solution or as a capsule. Radioactive iodine is rapidly incorporated into the thyroid gland and via its β-emissions produces radiation thyroiditis and fibrosis resulting in euthyroidism usually within 6-18 weeks [17]. Although obtaining euthyroidism while limiting hypothyroidism is the therapeutic ideal, it can rarely be achieved because radioactive iodine destroys both the hyperfunctioning thyroid cells as well as normofunctioning thyroid cells, so that most patients eventually develop hypothyroidism months after treatment. This expected outcome is taken care of with daily ingestion of levo-thyroxine tablet.

The average cost of this treatment is \$500 (N75000:00) and the cost of levo-thyroxine is less than \$2 (N300:00) a month. This is cheaper and more cost effective when compared with other modalities of treatment. Surgical intervention with the attendant risk of recurrence mortality and morbidity in the same hospital costs about \$1000 (N150000:00), while the antithyroid medication of the pair commonly used (carbimazole and propranol) which control the symptoms of excessive thyroid hormone costs \$5 (N750), in a month. Over an average of 20years for which most sufferers will use them amount to a whopping \$1200 (N180 000:00). It is worthy of note that the establishment of this facility attracted referrals from both surgical and medical arm of the spectrum of management. This implies acceptability of nuclear medicine management and indeed radioactive iodine ablation as a viable and effective option to patients, surgeons and clinician in our setting.

With the peak incidence of Graves' disease is in the 6<sup>th</sup> decade, at a time when the patients are becoming grandparents, coping with surgical

intervention or the recurrent popping of medication to control symptoms is undesirable. RAI therefore presents a readily acceptable option from which Graves' patients can now choose from.

Hospital stay on administration RAI is nil while post treatment follow up is non cumbersome. Complications arising from surgical intervention vary from heamorrhage to damage of recurrent laryngeal nerve. In the case of RAI therapy apart from radiation thyroiditis which is easily prevented by using secretagogues such as lime juice that encourage salivary glands contraction preventing storage of RAI, other complication are rare.

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