

Radioiodine Therapy for Hyperthyroidism

Abstract:

In the New England Journal of Medicine last year, Ross provided an excellent summary of current evidence on use of radioactive iodine (RAI) in the treatment of hyperthyroidism. However, clinical practice with regard to RAI treatment varies widely, with some key differences existing between the North American perspective provided by Ross and what is more widely practiced in Europe. Treatment of hyperthyroidism first requires an accurate diagnosis of the underlying aetiology. Hyperthyroidism refers to any condition in which there is an excessive production of thyroid hormone, which may arise from diffuse autoimmune stimulation in the case of Graves' disease (GD) or autonomously functioning nodules including toxic multinodular goitre (TMNG) and solitary toxic adenoma (TA). GD is the commonest cause of hyperthyroidism, but in areas of iodine deficiency the prevalence of TMNG and TA increase with age and therefore are more common than GD in older persons. Spontaneous remission occurs in approximately 30% of patients with GD, but is unlikely to occur in toxic nodules.

The rationale for RAI treatment is that iodine is a substrate for thyroid hormone synthesis and is actively transported into thyroid follicular cells, where thyroxine (T₄) and triiodothyronine (T₃) are formed and then stored within the colloid space. Radioiodine (¹³¹I) is similarly processed, and destruction of follicular cells is the result of β -particle radiation, effectively ablating functional thyroid tissue within a 1-2mm radius. A number of studies have provided reassurance with regard to the safety of RAI. The largest study included over 35,000 patients, followed for a mean of 21 years, and found that radioiodine was not linked to cancer mortality or any specific cancer

The main aim of RAI therapy is to eliminate the hyperthyroid state. However, for patients with GD there are philosophical differences in the approach used to achieve this goal. In the US the goal of RAI in GD is to render the patient hypothyroid. In contrast, the local practice in many Irish centres is to administer a dose of RAI calculated on the basis of an uptake scan with the intent of inducing a euthyroid state. The downside of this approach is that the incidence of persistent hyperthyroidism is higher and some patients may need a second treatment 6 months later. Most hyperthyroid patients will develop normal thyroid function within 4-8 weeks of treatment. Hypothyroidism can occur from 4 weeks, but more commonly arises between 2 and 6 months. For this reason, thyroid function is usually checked at 2, 4, and 6 months post-treatment, and less frequently thereafter. Thyroid stimulating hormone (TSH) levels may remain suppressed for several months following resolution of hyperthyroidism and should therefore be interpreted cautiously and only in association with free T₄ and T₃ levels. If thyroxine replacement is initiated, the dose should initially be guided by the free T₄ level. In contrast to GD, the approach to patients with TMNG or TA is generally the same world wide, namely to ablate only the adenoma(s). Provided that the TSH level is suppressed at the time of RAI, the incidence of post-ablative hypothyroidism is significantly less than for GD, as the suppressed normal tissue does not take up and concentrate RAI.

The decision when to use RAI versus one of the other effective treatments for hyperthyroidism, namely anti-thyroid drugs (ATDs) and surgery, depends on many factors, including clinician and patient preference, the underlying aetiology, patient age and co-morbidities, smoking status, presence of ophthalmopathy, and family issues such as planning pregnancy or young children at home. As highlighted in Ross' article, clinician preference for RAI varies greatly by location, with one study reporting that 69% of endocrinologists in North America recommend RAI as first-line therapy for GD, as compared with 22% of their European counterparts. In Europe, GD is usually managed with a trial of ATDs for 12-18 months, followed by a trial off drugs, and RAI therapy if hyperthyroidism recurs. Relapse usually happens within 6 months after discontinuation of drug, but can occur many years later. In cases of sub-clinical or mild hyperthyroidism, pretreatment with ATDs is usually not necessary. They may be used for a short period before RAI therapy, to alleviate symptoms in very thyrotoxic patients, or to reduce the small risk of a thyrotoxic crisis following the transient rise in circulating thyroid hormone that may occur. The use of carbimazole in this setting has no adverse effect on the time to cure or the success rate of RAI, provided it is discontinued 3-7 days before treatment.

While RAI is a safe and effective treatment, Ross emphasizes that there are important absolute contra-indications to its use including pregnancy, lactation, females planning a pregnancy within 4-6 months and an inability to comply with radiation safety guidelines. Thus, it is essential that a pregnancy test be obtained within 48 hours prior to treatment in any female with childbearing potential. All patients receiving RAI should be given explicit written information about the precautions required to avoid exposing others to unnecessary irradiation after treatment. This can be a particular issue with mothers of young children who may need to make special arrangements for several days following treatment. Patients should also be advised that ¹³¹I has a long half-life and can trigger airport security alarms for up to 12 weeks following treatment.

There is some controversy with regard to use of RAI in patients with Graves' ophthalmopathy (GO). Prospective, randomised, controlled trials have shown that RAI treatment is associated with a greater risk of the appearance or worsening of ophthalmopathy in GD patients, compared to treatment with an ATD or surgery secondary to an observed rise in TSH-receptor stimulating antibodies, peaking several months after RAI treatment. Smoking, high levels of pretreatment serum T₃ and post-RAI hypothyroidism are all associated with an increased risk of GO. On the other hand, prophylactic treatment with glucocorticoids can reduce the risk of deterioration of eye disease, with a recommended regimen of 0.5mg/kg/day prednisone, starting 3 days before RAI, continuing for 1 month, and then tapering over 2 months.

In summary, RAI is a safe and cost-effective treatment for hyperthyroidism, recommended as a first-line approach in TMNG and TA, and as a second-line therapy in non-smoking GD patients without ophthalmopathy, who relapse following a course of ATD. Physicians should discuss the three therapeutic options in detail, and ensure that in the case of RAI, the patient clearly understands the practical precautions required, and the potential for euthyroid, hypothyroid, or hyperthyroid outcomes.

J O'Connell, F Hayes
Department of Endocrinology, St Vincent's University Hospital, Elm Park, Dublin 4

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Comments: