

Treating Thyrotoxicosis with Radioiodine

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Abstract

Radioiodine, as a drug modality for the treatment of thyrotoxicosis, has been used in clinical practice for several decades. The physiologic basis, clinical indications and side-effects are discussed.

Ann Acad Med Singapore 2002; 31:542-4

Key words: Graves' disease, Hypothyroidism, Iodine-131, Toxic nodule

Introduction

Iodine is an essential component of thyroid hormone and is actively taken up by thyroid follicles. This is the physiological basis for the use of radioiodine in the treatment of thyrotoxicosis.

Radioiodine, radioactive iodine or iodine-131 refers to the same substance. It is essentially the mildly radioactive analogue of the naturally-occurring iodine found in our foodstuff (especially those from the sea). It has been used in clinical medicine since the 1940s in the treatment of Graves' disease (and some other types of thyrotoxicosis) as well as in differentiated thyroid carcinoma. It is supplied either in the form of a solution of sodium iodide and is a tasteless and odourless liquid medicine that can be dispensed, or it can be pre-packaged commercially into the form of capsules. The key to the understanding of the efficacy of radioiodine lies in the fact that it produces 2 types of weak radiation, namely, gamma radiation and beta radiation. The beta radiation is of therapeutic importance. It is low in energy and has very short path-lengths (travelling only about 1 to 2 mm in tissues) and therefore its effects are localised mainly to its target organ, which in this case is the thyroid gland. It causes cellular necrosis, reducing thyroid bulk and hence treating the thyrotoxicosis state. Numerous studies show that radioiodine is extremely safe. It has no biologic toxicity, a short half-life of only 8 days, and has a very well understood bio-distribution in the human body, concentrating mainly in the thyroid gland. Both its safety profile and its radiation dose profile are also very well understood. The dose of radioiodine administered is dependent on the weight (or size) of the thyroid gland which can be estimated clinically by palpation or

ultrasonography. The biologic clearance rate and the avidity of uptake of the iodine by the thyroid gland are also important considerations in the determination of the treatment dose. The goal is to deliver a 50 to 100 Gray radiation dose to the thyroid gland. In a loose sense, radioiodine therapy is a "functional" thyroidectomy.

Indications

The main indication for using radioiodine is failure of or recurrence after medical anti-thyroid drug therapy. Treatment of Graves' disease with anti-thyroid medication is associated with high rates of relapse. It is known that approximately 50% to 70% of patients with Graves' disease will relapse after completing a standard course of 1 to 2 years of anti-thyroid medication.^{1,2} This appears to be particularly true in those patients whose pretreatment examinations show a large goitre, more severe biochemical thyrotoxicosis, or the presence of thyroid stimulating hormone (TSH) receptor antibodies. The requirement of large doses of anti-thyroid drugs to control the thyrotoxic state and the inability to reduce the anti-thyroid dose over time also seem to predict poorer prognosis with medical therapy.³ Such patients will benefit from radioiodine. In some countries, such as the USA, radioiodine is also used for primary treatment of Graves' disease.

In addition, there are patients with definite, or even severe, allergic reactions to anti-thyroid medications (such as agranulocytosis or rash), or in whom time and prevention of long-term sequelae is of the critical importance (e.g., in some elderly patients, in those with thyrocardiac disease, or with recurrent periodic paralysis). Surgical management is also useful in many of these cases, especially if the goitre

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is producing distressing clinical symptoms or when there is a need to assess the thyroid for malignancy.

Medical treatment of toxic multinodular goitre or toxic adenoma is generally more difficult and will not produce permanent remission because the underlying pathogenetic mechanism is different, and radioiodine is also often useful in such cases. The 'toxic' nodule differentially takes up radioiodine more avidly than normal thyroid tissues and is selectively destroyed by it; hence, treating the thyrotoxicosis while the rest of the thyroid gland is relatively spared.

Treatment

For a few days prior to and up to several days after, the patient should avoid all seafood (including canned and processed foods) because they contain a significant amount of iodine. Multivitamins, cough mixtures and herbal drugs containing iodine should also be avoided. Amiodarone and iodinated contrast agents also contain relatively large amounts of iodine and radioiodine treatment should be postponed until at least 2 to 3 months after the cessation of these agents. They should also stop taking anti-thyroid medications for the same period of a few days as for seafood to increase the efficacy of the radioiodine.

Side Effects

Hypothyroidism

The main consequence of radioiodine therapy is post-therapy long-term hypothyroidism. As many as 90% of patients develop hypothyroidism within the first year,⁴ although results from a previous local study suggest about 50%.⁵ There is a recurrent risk of new cases of hypothyroidism of 1% to 5% annually. However, such long-term hypothyroidism is easily managed with thyroxine supplementation with no known long-term complications. Occasionally, *transient* hypothyroidism may occur about 2 months after the radioiodine therapy and may last for a few months.

Risk of Malignancies?

At the dose used to treat thyrotoxicosis, the risks of developing thyroid cancers, other solid organ malignancies or haematological malignancies are not significantly increased.⁶

Genetic Risk and Risk of Subfertility?

Genetic danger in offspring is always a concern among patients. However, they can be reassured. The ovarian dose is in the region of 0.2 rad/mCi or approximately 1 to 3 rads in a typical patient, an exposure similar in magnitude to the commonly performed radiological procedures such as barium enema or intravenous urogram (IVU). Several studies have been published which showed no significant increased risk of genetic abnormalities in children of

patients.⁷ Nevertheless, radioiodine is contraindicated in all pregnant women or whenever pregnancy is suspected. This is in view of the potential risk of congenital hypothyroidism and congenital malformations. It is also generally felt that pregnancy should be postponed for several months after radioiodine, that breast feeding should not be done as iodine is secreted into breast milk, and children should not be hugged for a few days. Mild increase in the incidence of miscarriages has been reported in the year or 2 after radioiodine therapy; although it is not established whether this is due to the radioiodine itself or to changes in thyroid hormonal status.⁸ Furthermore, this report was based on patients with thyroid carcinoma being given high doses of radioiodine. There is no long-term effect on fertility at the small doses used in thyrotoxicosis.

Graves' Dys thyroid Eye Disease

There is some controversy regarding the relationship between Graves' ophthalmopathy or orbitopathy and radioiodine treatment. In the majority of cases, no change in the status of the dysthyroid eye disease is noted⁹ but some reports noted a slight increase in the eye symptoms with radioiodine. Nevertheless, radioiodine is probably best avoided in patients with active Graves' ophthalmopathy. In patients with ophthalmopathy, a course of steroids has been shown to be protective.

Other Effects

The other minor acute side effects include mild nausea (possibly from radiation gastritis), neck discomfort (from radiation thyroiditis), transient change in taste sensation and some sialadenitis. These rarely last more than a few days. No drug allergy has been encountered with radioiodine, even among those who are allergic to iodinated contrast agents (the drug given is a very simple compound—sodium iodide—at the concentration of about 1 µg). Very rarely, there may be a transient exacerbation of the thyrotoxic symptoms due to release of pre-formed thyroid hormones leading to a thyroid storm state. This is most uncommon.

Clinical Monitoring

Radioiodine is given as an outpatient treatment and in the majority of cases, one treatment dose is sufficient. In a few patients, relapse occurs months later and a second dose of radioiodine is recommended. The thyrotoxicosis generally improves over a few weeks or months after radioiodine therapy. Follow-up is usually easy with monitoring of thyroid function and when hypothyroidism indeed occurs, treatment is relatively inexpensive with thyroxine tablets.

REFERENCES

1. Weetman A P. Graves' disease. *N Engl J Med* 2000; 343:1236-48.
2. Khoo D. Thyrotoxicosis. In: Ong Y Y, Woo K T, Ng H S, Tan P, Tang O T, editors. *A Clinical Approach to Medicine*. Singapore:

- World Scientific Publishing & SGH, 2001:264-77.
- Cooper D. Treatment of thyrotoxicosis. In: Braverman L E, Utiger R D, editors. *Werner & Ingbar's The Thyroid*. Philadelphia: Lippincott Williams & Wilkins, 2000:697.
 - Cunnen A J, Hay I D, Gorman C A, Offord K P, Scanlon P W. Radioiodine-induced hypothyroidism in Graves' disease: factors associated with the increasing incidence. *J Nucl Med* 1982; 23: 978-83.
 - Tavintharan S, Sundram F X, Chew L S. Radioiodine (I-131) therapy and the incidence of hypothyroidism. *Ann Acad Med Singapore* 1997; 26:128-31.
 - Ron E, Doody M M, Becker D V, Brill A B, Curtis R E, Goldman M B, et al. Cancer mortality following treatment for adult hyperthyroidism. Cooperative Thyrotoxicosis Therapy Follow-up Study Group. *JAMA* 1998; 280:347-55.
 - Sarkar S D, Beierwaltes W H, Gill S P, Cowley B J. Subsequent fertility and birth histories of children and adolescents treated with ¹³¹I for thyroid cancer. *J Nucl Med* 1976; 17:460-4.
 - Schlumberger M, De Vathaire F, Ceccarelli C, Delisle M J, Francese C, Couette J E, et al. Exposure to radioactive iodine-131 for scintigraphy or therapy does not preclude pregnancy in thyroid cancer patients. *J Nucl Med* 1996; 37:606-12.
 - Degroot L J. Radioiodine and the immune system. *Thyroid* 1997; 7:259-64.

QUESTIONS

- Regarding the clinical uses of radioiodine:
 - there is a role for it in the treatment of thyroid carcinoma.
 - it has been used for the treatment of subacute thyroiditis.
 - it can compete with naturally-occurring iodine for uptake in the thyroid follicles, thus reducing efficacy.
 - it can be used to treat toxic adenomas.
- When treatment with radioiodine is considered:
 - the patient should avoid taking fish for a few days.
 - admission to hospital is advised.
 - transient changes in taste may occur.
 - hypothyroidism may occur transiently or in the long term.
- Side effects of radioiodine include the following:
 - the majority will develop hypothyroidism.
 - the risk of haematological malignancy is increased.
 - breast feeding should be stopped for 1 week.
 - thyroiditis may develop transiently.
- Follow-up of treatment with radioiodine:
 - when relapse occurs, radioiodine should not be used for further treatment.
 - improvement in thyroid function tests is usually seen within a few days after treatment.
 - when hypothyroidism occurs, thyroxine supplementation is required usually for a few weeks.
 - radioiodine may be used as a primary therapy of Graves' disease.
- In the use of radioiodine for treatment of thyrotoxicosis:
 - amiodarone may affect the efficacy of radioiodine.
 - the size of the gland affects the dose of the radioiodine given.
 - the efficacy of the radioiodine is due to the weak beta radiation produced.
 - the long half-life of radioiodine increases the risk of genetic abnormalities in offspring.

ANSWER SHEET

Continuing Professional Development:
Clinical Update on Radioiodine

Question 1

- | | | | |
|---------|-----------------------|-------|-----------------------|
| a) True | ☐ | False | ☐ |
| b) True | ☐ | False | ☐ |
| c) True | ☐ | False | ☐ |
| d) True | ☐ | False | ☐ |

Question 4

- | | | | |
|---------|-----------------------|-------|-----------------------|
| a) True | ☐ | False | ☐ |
| b) True | ☐ | False | ☐ |
| c) True | ☐ | False | ☐ |
| d) True | ☐ | False | ☐ |

Question 2

- | | | | |
|---------|-----------------------|-------|-----------------------|
| a) True | ☐ | False | ☐ |
| b) True | ☐ | False | ☐ |
| c) True | ☐ | False | ☐ |
| d) True | ☐ | False | ☐ |

Question 5

- | | | | |
|---------|-----------------------|-------|-----------------------|
| a) True | ☐ | False | ☐ |
| b) True | ☐ | False | ☐ |
| c) True | ☐ | False | ☐ |
| d) True | ☐ | False | ☐ |

Question 3

- | | | | |
|---------|-----------------------|-------|-----------------------|
| a) True | ☐ | False | ☐ |
| b) True | ☐ | False | ☐ |
| c) True | ☐ | False | ☐ |
| d) True | ☐ | False | ☐ |

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