

# Effectiveness Of Fixed Dose Radioactive Iodine (Rai) For The Treatment Of Thyrotoxicosis : A United Kingdom District General Hospital Experience

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## Abstract

There is no consensus on the most appropriate way of prescribing the dose of radioactive iodine (RAI) to treat thyrotoxicosis. In recent years, the trend is favouring a simple fixed dose regime. We conducted a pilot audit in 2002 on 40 thyrotoxic patients who received either 7 mCi or 11 mCi RAI in 1995 and 1996 in a district general hospital in England, United Kingdom. Results showed no statistical difference between 7mCi and 11mCi RAI, in all clinical variables examined. The apparent higher cure rate for 7mCi was likely due to more of the "iller" patients ( e.g. larger goitre) receiving 11mCi. Patients with nodular goitre (NG) and large goiter may need more than 11mCi. Overall cure rate was 83%. We concluded that fixed standard doses of RAI is a cost effective and efficient way of administering RAI for the treatment of thyrotoxicosis.

## INTRODUCTION

There has been little consensus on the most appropriate dose of RAI (  $^{131}\text{I}$  ) to treat thyrotoxicosis. Choices include fixed doses <sup>1345</sup> and calculated doses based on a formula incorporating thyroid size, uptake and turnover of RAI <sup>678</sup> . A previous survey suggests that many physicians use some form of a dose adjustment approach, although it is uncertain whether this leads to improved clinical outcomes. <sup>9</sup> Different aetiologies of thyrotoxicosis may also require different doses of RAI although opinions vary on this as well. <sup>51314</sup> We conducted a pilot audit on 40 thyrotoxic patients who received RAI in 1995 and 1996 in a district general hospital in England, United Kingdom.

## AIMS

- (1) To determine the cure rates of 7 mCi versus 11 mCi 6 years post RAI
- (2) To examine the impact of aetiologies (Graves' disease versus nodular goitre (NG)), age, gender and goitre size on the cure rates (defined as euthyroidism or hypothyroidism)

## MATERIALS AND METHODS

150 patients who had RAI in 1995 and 1996 were identified from Nuclear Medicine records. Patients' medical notes were obtained from Medical Records and these details were examined : age at diagnosis, sex, aetiology of thyrotoxicosis,

goitre presence, size and type, dose and frequency of RAI and outcome of RAI.

Postal questionnaires requesting information regarding their latest thyroid function result were sent to their general practitioners (GPs) from February to May 2002. A response rate of 29.3% (44 GPs) replied with the required information. 4 patients were excluded; 3 had prior treatment with either RAI or thyroidectomy before the study period and we do not know the dose of RAI given in 1 patient.

Patients were categorized, by clinical and immunological criteria, into 2 groups : Graves' disease and toxic nodular goiter. Graves' disease was diagnosed as the presence of biochemical thyrotoxicosis (raised free T4, suppressed TSH), absence of nodular goitre and either the presence of thyroid autoantibodies or thyroid eye disease. Toxic nodular goitre is diagnosed as thyrotoxicosis in a palpable nodular goitre. We did not evaluate the possibility of Graves' disease on a background of nodular goitre, for the purpose of this audit.

Patients either had 7 mCi or 11 mCi. Most patients had their RAI treatment under the clinical oncologists at the Royal Berkshire Hospital although 2 patients had theirs at Oxford. Anti-thyroid drugs (ATD), if given, were usually withdrawn 3 days before RAI. These patients were then seen 6 weeks later in the endocrine clinic with a repeat thyroid function

test (TFT). TFTs were then repeated at regular intervals at the discretion of the clinicians. Persistent thyrotoxicosis would need recommencement of ATD. Repeat RAI may be considered after 6 months. Hypothyroidism would be treated with thyroid hormone replacement.

Cure after RAI was defined as euthyroidism off all ATDs or hypothyroidism needing thyroxine replacement.

## STATISTICS

The chi-square was used to test for association between 2 categorical factors. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL, United States).

## RESULTS

Table 1 showed the comparison of cure rates between 7 mCi and 11 mCi, and the influence of aetiologies, goitre size, gender and age on the cure rates. None of the patients with NG or with a moderate or large goitre received the lower dose. Patients who were female, had a diagnosis of MNG (not Graves' disease), those with a goitre and those aged 65 years or older were more likely to receive 11 mCi. They were also less likely to be cured.

Our audit showed that, 6 years post RAI, the overall cure rate was 83% (89% and 77% for those prescribed 7 mCi and 11 mCi respectively). Overall the percentage cured was higher for 7mCi, although not statistically significant ( $X^2 = 0.9$ ;  $p=0.34$ ). However, this difference depended on the category of patients and in the case of patients aged 65 years and older, the trend was reversed. Lower cure rates were noted in NG and in moderate-large goitre despite having 11 mCi. None of the differences in cured rates between the 7 and 11 mCi were statistically significant.

We were unable to obtain accurate documentation regarding the severity of hyperthyroidism at presentation and use of ATDs pre- and post- RAI, hence these variables were not analysed.

**Figure 1**

Table 1: Comparison of cure rates between 7 mCi and 11 mCi and influence of aetiologies, goitre size, gender and age

Category	Total No. of patients	% 11 mCi	% cured	Subgroup within category	Dose of RAI (mCi)	No. of patients	% cured
All	40	55%	83%	All	7 11	18 22	89% 77%
<u>Diagnosis</u>							
Graves	31	48%	84%	Graves	7	16	88%
NG	6 (NA=3)	100%	67%	NG	11 7 11	15 - 6	80% - 67%
<u>Goitre Size</u>							
None	21	38%	86%	None	7	13	85%
Small	8	62%	88%	Small	11 7	8 8	88% 100%
Moderate/Large	8 (NA=3)	100%	63%	Mod/Large	11 7 11	3 - 8	80% - 63%
<u>Age in years</u>							
<45	11	73%	91%	<45	7	3	100%
45-64	16	31%	88%		11	8	88%
≥65	13 (NA=2)	73%	73%	45-64	7 11	11 5	91% 80%
				≥65	7 11	3 8	67% 75%
<u>Sex</u>							
Male	5	40%	100%	Male	7	3	100%
Female	35	57%	80%	Female	11 7 11	2 15 20	100% 87% 75%

NA= data not available

## DISCUSSION

Several studies have shown that fixed dose regime is as effective, if not more, than calculated-dose methods, in terms of improving cure rates or avoiding hypothyroidism.

A prospective randomized trial which compared standard (555 MBq) (1 mCi = 37 MBq) versus calculated iodine-131 activity (to deliver 100Gy, taking into consideration thyroid volume by ultrasound and radioiodine kinetics) for Graves' hyperthyroidism found higher success rates (defined as elimination of hyperthyroidism 6 months

posttreatment) with fixed activity (71%) vs. adjusted activity (58%), a difference that was marginally significant ( $P = 0.05$ ). The median activity given to the adjusted dose group was 298 MBq, which prevents direct comparison with outcome results from the fixed dose of 555 MBq.<sup>10</sup> In another open randomized trial, 221 consecutive hyperthyroid patients were randomized to receive a fixed dose of iodine-131 (185, 370, or 555 MBq depending upon gland size) or an individualized dose (3.7 MBq/g total thyroid volume by ultrasound adjusted for 24-h radioiodine uptake measurement, to a maximum dose 740 MBq).<sup>11</sup> No significant difference in outcome was found between the 2 regimes. The researchers concluded that a semiquantitative approach is probably as good as using more elaborately calculated radioiodine doses and is more cost effective. Similar conclusion was reached in a Hong Kong study of 149 patients with thyrotoxicosis who were given 200 MBq, 250 MBq and 300 MBq (commonest) RAI.<sup>15</sup> Contrary to previous reports,<sup>13,14</sup> a recent 1-year follow-up study comparing fixed dose versus calculated dose showed similar outcomes in Graves' disease and MNG, thereby concluding that thyrotoxicosis could be treated with a standardized regime, minimizing patient inconvenience and improving procedure efficiency.<sup>5</sup>

Many studies have shown that RAI failure is associated with large goitre size, severe hyperthyroidism at presentation, male and younger patients.<sup>112</sup> There have been contradictory reports regarding the use of ATDs pre- and post RAI as a prognostic marker.<sup>115</sup> These results have been shown to support the practice of using a "sliding scale" of standardized doses. The limitation of the small sample size of our audit made it difficult to draw meaningful conclusions about prognostic factors for each subgroup of patients. Nevertheless, the results indicated that some, if not all, of the apparent higher cure rate for 7mCi was likely due to more of the "iller" patients (e.g. larger goitre) receiving 11mCi. The lower cure rates in MNG and large goitre despite receiving 11 mCi suggested that higher dose(s) should be considered.

Our audit is one of the few which looked at outcome more than 5 years post RAI treatment. The high overall cure rates seen in our audit, higher than previously reported, probably reflects the cumulative incidence of hypothyroidism that occurs over time.

## CONCLUSION

Standard fixed doses of RAI have a good cure rate for

thyrotoxicosis. It is a cost effective and efficient way of administering RAI for the treatment of thyrotoxicosis.

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