MedCrave
Step into the World of Research

Endocrinology & Metabolism International Journal

Research Article

Open Access

CrossMark

Outcomes following fixed dose radioactive iodine therapy (RAI) in hyperthyroid patients with grave's disease and toxic nodular disease

Abstract

Background: Radioactive iodine (RAI) is a definitive treatment for hyperthyroidism, but administered doses vary between institutions. We utilize a fixed dose RAI treatment protocol, administering 370MBq to all patients unless there is a large goitre present. We aimed to determine treatment outcomes following fixed dose RAI at our centre.

Methods: We retrospectively reviewed thyroid function at 1 year following RAI therapy in 166 consecutive hyperthyroid patients who had been treated with 370MBq RAI between January 2001 and March 2015. Patients were stratified into 2 aetiological groups: Grave's disease (GD) and toxic multinodular goitre (TMNG)/toxic adenoma (TA) for comparison.

Results: 166 patients received 370MBq RAI over the period specified. 88 patients had GD (53%) and 70 patients had TMNG/TA (42%). Aetiology was not specified in 8 patients (5%). Patients with GD were younger 46.1±1.5 years (mean±SEM)) compared to those with TMNG/TA (63.3±1.4 years, $p<0.001$) and there were more female than males in both groups (80% female in GD and 84% in TMNG/TA, $p=0.445$). At one year post-RAI, more patients with GD were rendered hypothyroid compared to TMNG/TA (55% vs. 17%) and fewer patients with GD were rendered euthyroid (34% vs.63%) or had persistent hyperthyroidism compared to those with TMNG/TA (11% vs 20%) ($p<0.001$).

Conclusion: When compared to GD group, proportionally more TMNG/TA patients remained hyperthyroid a year following a single dose of 370Mbq RAI. TMNG/TA patients were more likely to be euthyroid at one year post RAI, however. These results suggest that a higher dose of RAI may be needed for TMNG/TA.

Keywords: outcome, fixed dose, radioactive iodine, hyperthyroid, hypothyroidism, nodular thyroid disease

Volume 3 Issue 6 - 2016

Seong Keat Cheah,[1] Khaled Aljenaee,[1] Nazri Muhammad,[1] Linda Gavigan,[2] Maria Dooley,[2] Seamus Sreenan,[1] Tommy Kyaw Tun,[1] John McDermott[1]

[1]Department of Endocrinology, Connolly Hospital, Ireland
[2]Department of Medical Physics, Beaumont Hospital, Ireland

Correspondence: Seong Keat Cheah, Department of Endocrinology, Connolly Hospital, Blanchardstown, Dublin 15, Irish Republic, Ireland, Tel +353851583387, Email seongkeatc@gmail.com

Received: November 04, 2016 | **Published:** December 19, 2016

Abbrevations: RAI, radioactive iodine; GD, grave's disease; TMNG, toxic multinodular goitre; TA, toxic adenoma; ATA, american thyroid association

Introduction

Oral administration of radioiodine (I131) is a safe and cost-effective treatment option for patients with toxic multinodular goitre/toxic adenoma or Grave's diseas.[1] Radioiodine (RAI) has been used since 1940 and achieves excellent cure rates for hyperthyroidism with minimal side effects and complications.[2-4] Debate ensues over whether a fixed dose of RAI or a variable individualized dose based on the size of thyroid gland size and/or 24-hour radioiodine uptake and turnover should be used.[5,6] In particular it has been suggested that a lower dosage of RAI should be used to limit rates of hypothyroidism post RAI.[6] However such an approach has been associated with higher rate of treatment failure and hence most experts advocate higher dose RAI with the aim of rendering patients hypothyroid in order to be certain of cure for hyperthyroidism with a single dose of RAI.[7]

It is important to take into account the aetiology of hyperthyroidism when considering whether one should attempt to individualize the RAI dose to achieve the desired treatment outcome. The therapeutic effect of RAI varies depending on the aetiology of the hyperthyroidism, with GD more commonly rendered hypothyroid, while more patients with TMNG/TA are rendered euthyroid post-RAI. Higher doses of RAI increase the RAI success rate and the incidence of hypothyroidism. This was demonstrated in a trial comparing 2 different fixed doses of RAI (370MBq vs 185MBq) for the treatment of 813 hyperthyroid. In the 370MBq treatment group, an 85% cure rate was achieved but 61% of the patients had hypothyroidism. This compares with a 67% cure rate and 41% hypothyroidism rate in the 185MBq treatment group.[8] However this study did not show any difference between the cure rates based on aetiology.

The American Thyroid Association (ATA) guidelines recommend a dose of RAI sufficient to cause hypothyroidism, typically 370 to 555MBq for GD, and that 370 to 740MBq for TA. Only for TMNG a variable dose of 5.55-7.4MBq per gram of tissue corrected for RAI uptake should be given.[7] The provided range is wide and subject to the prescribing clinician's experience and preference. Some clinicians apply only a clinical estimation of thyroid gland size to decide on RAI dosage. Our study was designed to examine the RAI outcome as indicated by thyroid status at one year after administration of fixed dose RAI at the lowest recommended dosage of 370MBq for both GD and TMNG/TA.

Materials and methods

Standard of care

Our institution utilizes a fixed dose of 370MBq RAI for hyperthyroidism treatment regardless of aetiology, unless there is a clinically large goitre. This corresponds with the lower recommended dose within the range proposed by the ATA. For those who were on oral anti-thyroid medication prior to RAI, discontinuation was advised at least 5 days prior to RAI. This is in accordance with the findings from a metaanalysis that recent methimazole and propylthiouracil administration is known to lower RAI treatment success rate.[9] All patients receiving RAI were provided with written advice regarding radiation safety precautions following treatment.[7] Post treatment, patients were followed with repeat thyroid function tests 6 weekly for 6 months, and at longer intervals thereafter.

Study design

We retrospectively reviewed outcomes following RAI therapy in hyperthyroid patients attending our centre who had received 370MBq RAI between January 2001 and March 2015. The RAI therapy was administered by Nuclear Medicine Department, Beaumont Hospital, Dublin. The patients were stratified into two groups, GD and nodular thyroid disease (TMNG/TA), and thyroid status was determined at one year post RAI in order to determine treatment outcomes. The diagnosis of GD was supported with the presence of thyroid autoantibodies (namely anti-TSH receptor antibody), and/or presence of typical features such as a diffuse goitre and/or the presence of thyroid eye disease, and/or typical findings on technetium scan. The diagnosis of TMNG/TA was supported by sonographic findings or documented nodular goitre on clinical palpation and/or typical findings on technetium scan. Euthyroid state was defined biochemically as TSH level between 0.27-4.20mU/L as per local laboratory reference range, in patients not taking concomitant thyroxine or anti-thyroid medication. Hypothyroid state was defined either biochemically as TSH level >4.20mU/L as per local laboratory reference without concomitant anti-thyroid medication, or on the basis of a requirement for thyroxine replacement. Persistent hyperthyroidism was defined either biochemically as a TSH level <0.27mU/L as per local laboratory reference range without concomitant thyroxine replacement, or on the basis of a requirement for anti-thyroid medication.

Statistical analysis

Differences between categorical variables (expressed as number and percentages) were assessed using Chi-square test. Differences between continuous variables were evaluated with independent sample t-test (equal variances assumed as per Levine's test). Values of $p<0.05$ were considered statistically significant. IBM SPSS software version 23 was used for statistical analysis.

Results

During the specified period, we identified 183 hyperthyroid patients who had received RAI consecutively. 166(91%) patients had received 370MBq, 2(1%) patients 400MBq, 10(5%) 500MBq, 4(2%) 550MBq, and 1(1%) 600MBq. Only patients receiving 370MBq were included in subsequent analysis.

Of these 166 patients who received 370MBq RAI, 88 (53%) were diagnosed as having GD while 70 (42%) were diagnosed as having TMNG/TA. In 8 (5%) patients the aetiology of their hyperthyroidism was not specified and these patients were excluded from subsequent analysis.

As depicted in Table 1, the GD group were on average 17.2 years younger than the TMNG/TA group (P<0.001). There was a female preponderance of patients in groups, 80% for GD and 84% for TMNG/TA.

At one year post-RAI, 48(55%) patients with GD were rendered hypothyroid as opposed to 12(17%) TMNG/TA patients. 30(34%) patients with GD were euthyroid, compared to 44(63%) patients with TMNG/TA. Treatment failure as defined as hyperthyroid state at one year post-RAI was found in 10(11%) patients with GD and 14(20%) with TMNG/TA.

Table 1 RAI outcome at 1 year

		GD		TMNG/TA		p-value
Number of Patients		88		70		
Age (Mean±SEM, Years)		46.1±1.5		63.3±1.4		P<0.001[a]
		n	%	n	%	
Gender	Female	70	80	59	84	p=0.445[b]
	Male	18	20	11	16	
Thyroid Status (1y post-RAI)	Hypothyroid	48	55	12	17	P<0.001[c]
	Euthyroid	30	34	44	63	
	Hyperthyroid	10	11	14	20	
Thyroid Eye Disease	No	63	72	64	91	p=0.002[d]
	Yes	25	28	6	9	

[a]independent sample t-test, [b]Chi-square test, $X^2=0.585$ (df=1, p=0.445), [c]Chi-square test, $X^2=23.165$ (df=2, p=0.000), [d]Chi-square test, $X^2=9.729$ (df=1, p=0.002).

Citation: Cheah SK, Aljenaee K, Muhammad N, et al. Outcomes following fixed dose radioactive iodine therapy (RAI) in hyperthyroid patients with grave's disease and toxic nodular disease. *Endocrinol Metab Int J.* 2016;3(6):174–176. DOI: 10.15406/emij.2016.03.00070

Discussion

Sustained euthyroidism without the need for ongoing medical therapy would clearly be the most desirable RAI treatment outcome. This is difficult to achieve, however, as overzealous dosing of RAI leads to high rates of hypothyroidism as reported in most series, while under-dosage of RAI aiming for euthyroid state will lead to an increase in treatment failure rate. The ATA recommends a wide range of RAI dosage for clinicians administering RAI, with recommended doses ranging from 370-555MBq for GD and 370-740MBq for TMNG/TA. This recommendation provides liberty to prescribing clinicians to opt for doses according to individual centre experience and clinical estimation of thyroid volume. Administering the lower range of this dosage (370MBq) in our patients results in a failure rate that is higher in TMNG/TA by almost two-fold compared to GD. A euthyroid state was restored in our TMNG/TA group almost 2-fold more often than in our GD group, however, while a hypothyroid state was more prevalent in GD group by 3-fold. Patients with TMNG/TA may opt for our low fixed dose of RAI in the knowledge that, while repeat treatment may be necessary in the event of treatment failure, in almost two thirds of cases the perfect outcome of euthyroid state was achieved at one year post-treatment.

Our treatment outcomes reflect outcomes in a general population of hyperthyroid patients where sonographic or radioiodine uptake estimation of thyroid volume was not performed routinely and where clinical examination only for an obviously large goitre was used to determine suitability for fixed dose 370MBq RAI. The effect of thyroid size on RAI treatment outcome is well established, with an inverse relationship between thyroid size and the success rates of the RAI therapy.[10] In a prospective, randomized trial comparing a fixed dose with a calculated dose the success rate was lower in the fixed dose group in patients with large goiters-success rates ranged from 100% for patients with thyroid volumes ≤15mL to only 25% in patients with volume ≥75mL [10]. In a randomized trial comparing four RAI doses (low fixed, high fixed, low calculated, high calculated) in 88 patients with GD based on thyroid size estimation, fixed doses of 6.4mCi (235MBq) or 9.4mCi (350MBq) were as effective as low-or high-calculated doses (80 or 120microCi/g), supporting the applicability of the fixed dose approach[11]

Conclusion

In conclusion, a fixed dose RAI approach is convenient and achieves comparable outcomes to a calculated dose RAI approach. However, an individualized approach is paramount to achieve a desirable outcome, and our findings demonstrate that a fixed dose of 370MBq applied to all patients unless there is a clinically obvious large goitre will result in different outcomes between GD and TMNG/TA patients. As reported in other series, TMNG/TA are more likely to be rendered euthyroid post RAI at the expense of higher failure rate, compared to GD. Patient education regarding treatment outcomes in order to allow for greater patient choice regarding RAI doses is important.

Acknowledgment

We thank Beaumont Hospital Nuclear Medicine Department providing RAI therapy to this cohort of patients.

Conflicts of interest

The author declares there is no conflict of interest.

References

1. Ross DS. Radioiodine Therapy for Hyperthyroidism. *N Engl J Med.* 2011;364(6):542–550.
2. Reiners C, Schneider P. Radioiodine therapy of thyroid autonomy. *Eur J Nucl Med Mol Imaging*. 2002;29(Suppl 2):S471–S478.
3. Franklyn JA, Maisonneuve P, Sheppard MC, et al. Mortality after the Treatment of Hyperthyroidism with Radioactive Iodine. *N Engl J Med.* 1998;338(11):712–718.
4. Stokkel MPM, Handkiewicz Junak D, Lassmann M, et al. EANM procedure guidelines for therapy of benign thyroid disease. *Eur J Nucl Med Mol Imaging.* 2010;37(11):2218–2228.
5. Abraham P, Acharya S. Current and emerging treatment options for graves' hyperthyroidism. *Ther Clin Risk Manag.* 2010;6(1):29–40.
6. Wood AJJ, Franklyn JA. The Management of Hyperthyroidism. *N Engl J Med.* 1994;330(24):1731–1738.
7. Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. *Thyroid.* 2016;26(10):1343–1421.
8. Allahabadia A, Daykin J, Sheppard MC, et al. Radioiodine treatment of hyperthyroidism–prognostic factors for outcome. *J Clin Endocrinol Metab.* 2001;86(8):3611–3617.
9. Walter MA, Briel M, Christ–Crain M, et al. Effects of antithyroid drugs on radioiodine treatment: systematic review and meta–analysis of randomised controlled trials. *BMJ.* 2007;334(7592):514.
10. Peters H, Fischer C, Bogner U, et al. Radioiodine therapy of Graves' hyperthyroidism: standard vs. calculated 131 iodine activity. Results from a prospective, randomized, multicentre study. *Eur J Clin Invest.* 1995;25(3):186–193.
11. Leslie WD, Ward L, Salamon EA, et al. A randomized comparison of radioiodine doses in Graves' hyperthyroidism. *J Clin Endocrinol Metab.* 2003;88(3):978–983.

Citation: Cheah SK, Aljenaee K, Muhammad N, et al. Outcomes following fixed dose radioactive iodine therapy (RAI) in hyperthyroid patients with grave's disease and toxic nodular disease. *Endocrinol Metab Int J.* 2016;3(6):174–176. DOI: 10.15406/emij.2016.03.00070