

SF Journal of Endocrinology and Thyroid

Outcomes Post Radioactive Iodine Therapy (RAI) in Hyperthyroid Patients with Graves' Disease and Toxic Nodular Disease

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Abstract

Background: To evaluate the success rate of therapeutic administration of a single calculated ¹³¹I activity for eliminating hyperthyroidism due to Graves' disease and autonomous thyroid nodules.

Methods: Clinical records were retrospectively reviewed for patients with hyperthyroidism between September 2016 and March 2019 who received Radioactive Iodine (RAI) thyroid gland ablation therapy as definitive treatment of hyperthyroidism. Patients were divided to 2 groups, Graves' disease (GD) and Toxic Multinodular Goiter (TMNG) /Thyroid Adenoma (TA). An average dose of 5-7 MBq/g was given with response to therapy assessed at 6 months, clinically and with biomedical follow up.

Results: Total of 68 hyperthyroid patients who had received RAI were identified, 49 patients with Graves' disease patients (72%) and 19 patients with TMNG/TA (18%). On average, GD group were younger by 13 years and a female predominance was noted in both groups. At 6-months post-RAI, patients with Graves' disease received an average dose of 370-750 MBq based on clinical assessment or fixed, with a cure rate of 94% (90% hypothyroid, 4% euthyroid). On the other hand, patients with TMNG/TA received calculated dose of 410-960 MBq based on thyroid volume and 24-hour thyroid uptake. An 89% success rate was achieved (78% hypothyroid, 11% euthyroid).

Conclusion: Radioactive iodine therapy is a potent treatment of hyperthyroidism. Further efforts must be directed at curing disease while achieving an euthyroid state for optimal patient outcome.

Keywords: Hyperthyroidism; Radioactive iodine; Calculated dose

Abbreviations

RAI: Radioactive Iodine; GD: Graves' disease; TMNG: toxic multinodular goiter; TA: thyroid adenoma

Introduction

Hyperthyroidism is characterized by increased thyroid hormone synthesis and secretion from the thyroid gland, most commonly due to Graves' disease and autonomous thyroid nodules. There are three options for treating patients with hyperthyroidism; Antithyroid Drugs (ATDs), Radioactive Iodine ¹³¹I (RAI) ablation, and surgery [1].

Radioactive Iodine ¹³¹I (RAI) treatment is an effective definitive treatment of hyperthyroidism and has been available since the 1940s [2] ¹³¹I being selectively concentrated by functioning thyroid tissue that is subsequently destroyed over weeks to months by beta-radiation [3].

The optimum radioactive iodine dose is debated and varies among institutions between a fixed dose versus a dose calculated on the basis of thyroidal radioiodine uptake, but several studies found no significant differences in treatment outcomes and in rates of permanent hypothyroidism between the two regimens [1].

In our Hospital the calculated dose protocol depends on the 24-hour thyroid uptake scan and has been used over the last 3 years. The objective of this study is to evaluate and share the success rate of therapeutic administration of a calculated ¹³¹I dose for treating Graves' disease and autonomous

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Received Date: 27 Jun 2020

Accepted Date: 10 Jul 2020

Published Date: 16 Jul 2020

Citation: Owayed S, Alshatti K, Hajji S, Aljenaee K. Outcomes Post Radioactive Iodine Therapy (RAI) in Hyperthyroid Patients with Graves' Disease and Toxic Nodular Disease. *SF J Endocrinol Thyroid*. 2020; 1(1): 1004.

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thyroid nodules.

Methods and Materials

Standard of care

Our institution utilizes a calculated dose of RAI for hyperthyroidism treatment regardless of aetiology (5-7 MBq/g), this corresponds with the mid-high 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 7 days prior to RAI. All patients receiving RAI were provided with written advice regarding radiation safety precautions following treatment. Post treatment, patients were followed with repeat thyroid function tests every 4 weeks for 6 months, and at longer intervals thereafter.

Study design

We retrospectively reviewed outcomes following RAI therapy in hyperthyroid patients attending our institution who had received calculated dose RAI between September 2016 and March 2019. The RAI therapy was administered by the Nuclear Medicine Department, Adan Hospital, Kuwait. The patients were stratified into two groups, GD group and nodular thyroid disease (TMNG/TA) group, and thyroid status was determined at 6 months 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 typical findings on technetium scan. The diagnosis of TMNG/TA was supported by typical findings on technetium scan. Euthyroid state was defined biochemically as TSH level between 0.25-4.6 mU/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 >4.6 mU/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 <0.25 mU/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 24 was used for statistical analysis.

Results and Discussion

During the specified period, we identified 68 hyperthyroid patients who had received RAI consecutively. As depicted in Table 1, 49/68 patients had GD (72%) and 19/68 TMNG/TA (18%). The GD group were on average 13 years younger than the TMNG/TA group ($P < 0.001$). There was a female preponderance of patients in both groups, 61% for GD and 75% for TMNG/TA. Patients within Graves' disease group received as estimated dose based on clinical assessment or fixed dose (370-750 MBq), while patients in TMNG/TA group received calculated dose based on thyroid volume and 24-hour thyroid uptake (410-960 MBq).

At 6-months post-RAI, 44 (55%) patients with GD were rendered hypothyroid as opposed to 16 (78%) TMNG/TA patients. 2 (4%) patients with GD were euthyroid, compared to 2 (11%) patients with TMNG/TA. Treatment failure defined as hyperthyroid state

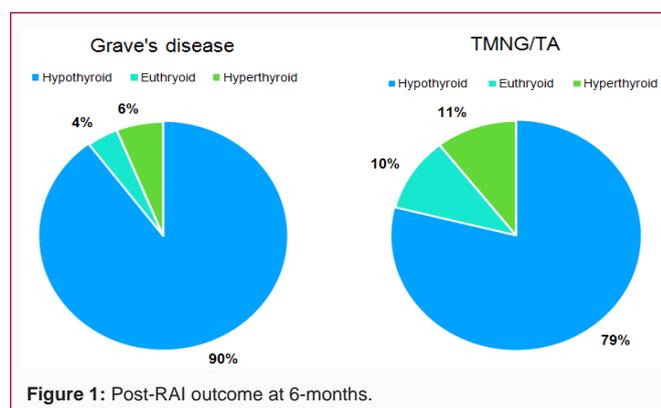


Table 1: Patients' characteristics and post-RAI outcome at 6-months.

	GD	TMNG/TA	p-value
Number of patients	49	19	
Age (median)	38	51	<0.005
Gender:			
Male	22 (45%)	5 (26%)	0.174
Female	30 (61%)	15 (75%)	-
24-hour thyroid uptake (median)	63.295	51.5	<0.005
Dose in MBq (median)	568.505	731.12	<0.005
Thyroid status (6 months post RAI)			
Hypothyroid	44 (90%)	15 (78%)	<0.005
Euthyroid	2 (4%)	2 (11%)	-
Hyperthyroid	3 (6%)	2 (11%)	-

at 6-months post-RAI was found in 3 (6%) patients with GD and 2 (11%) with TMNG/TA. Data is summarized in Figure 1.

Radioiodine therapy has been a definitive treatment for hyperthyroidism for over 50 years [4]. During this time there has been much debate on the dosing of treatment, high versus low dose, and fixed versus calculated dose of radioiodine.

In terms of dosing of radioiodine therapy, though it may be tempting to give patients a lower dose of therapy to induce an euthyroid state, the American Thyroid Association states that the goal of treatment is to cure hyperthyroidism. This is achieved by rendering the patient hypothyroid; thus, an adequate dose of radiation is required [5].

Different strategies exist for the calculation of radioiodine administered to patients. Fixed dose calculation is administering a predetermined dose of therapy irrespective of gland size and iodine uptake. Doses typically given are 5, 10, or 15 mCi (185, 370, or 555 MBq) [4,6,7]. Individual dosing, however, is calculated using these variables. The size of the gland is estimated clinically or by imaging and iodine uptake is by 24-hour iodine uptake before treatment [7].

The main purpose of this study is to share our experience in Adan Hospital, Kuwait. Hyperthyroid patients were divided to two groups, Grave's disease group and TMNG/TA group. Those with Grave's disease received an estimated dose based on clinical evaluation or fixed dose, while TMNG/TA group received a calculated dose. Cure rate for Grave's disease was found to be 94% and for TMNG/TA 89% at 6-months post radioiodine therapy.

When matching up our data with other data in the region around us (Table 2) using the same methods of determining the dose, we find that our center has a higher cure rate, however as a consequence we report a higher rate of hypothyroidism (Graves' disease 89.9%,

Table 2: Comparison of Post-RAI in the region.

Institute	Disease	No. of patients	Dose received (mCi)	Post-radioiodine outcomes at 6 months		
				Hypothyroid	Euthyroid	Hyperthyroid
Adan Hospital, Kuwait, present study	GD	49	15.4 fiD/esD	89.8%	4.1%	6.1%
	TMNG/TA	19	19.8 calD	79%	10.5%	10.5%
Tawam Hospital, UAE, 2019 [8]	GD	97	14.7±3.7 calD	80.6%	11.9%	7.5%
	TMNG		13.7±3.5 calD	65.2%	26.1%	8.7%
	TA		16.7±3.9 calD	33.3%	33.3%	33.3%
Salmaniya Medical Complex, Bahrain* 2019 [9]	GD	118	15 fiD	88.2%	4.4%	7.4%
	TMNG	11				
	TA	7				
King Abdulaziz University Hospital, 2009 [10]	-	73	10 fiD	26%	59%	4%
Hamad Medical Corporation, Qatar 2009 [11]	GD	85	10 for small goiter 15 for large goiter	62.4%	22.4%	15.3%
	TMNG	13		84.6%	7.7%	7.7%
	TA	6		50%	16.7%	33.3%
Sultan Qaboos University Hospital, Oman* 2002 [12]	GD	366	9.5-16.2 fiD	85.5%	2.5%	12%

*Patients were followed up to 12 months post radioiodine therapy fiD = fixed dose, esD = estimated dose, calD = calculated dose

TMNG/TA 79%).

In the UK, a ten-year retrospective study evaluated the efficacy of fixed doses of 10 mCi versus 15 mCi. The overall success rate was 90% for both doses [8-13]. This is similar to our rate, and in agreement with the literature that there is no major difference between the calculated and fixed dose method of radioiodine therapy.

Furthermore, ethnicity is a variable one must consider. In West Africa, retrospective analysis of consecutive hyperthyroid patients treated with radioiodine was done. All patients received a Tc-99m per technetate thyroid scan before therapy. Doses were 15-30 mCi. Empirical dosing, with a minimum of 10 mCi, was administered per patient. Patients with large glands, nodular glands, and patients for retreatment received higher doses of 30 mCi. At 6 months following RAI therapy, 77.8% of patients had developed euthyroidism or hypothyroidism, confirming that patients with African descent are more resistant to treatment with radioiodine [14].

Conclusion

Radioactive iodine therapy is a safe definitive treatment of hyperthyroidism. In Adan Hospital, Kuwait, the cure rate for Graves' disease and TMNG/TA is 94% and 89% respectively. This rate comes at the expense of a higher incidence of hypothyroidism. Our aim in the future is to improve patient outcome and reduce this incidence, with the possibility of introducing different strategies for calculating the dose of radioiodine therapy such as dosimetry.

Author Contributions

SH and K Aljenaee designed the study. K Alshatti collected the data of the study. SO, SH, and K Aljenaee analyzed and interpreted the data. SO is the primary author and wrote the manuscript. All authors reviewed the final manuscript.

Acknowledgments

We would like to gratefully acknowledge Esraa Alqattan and Iman Alshammeri of the Nuclear Medicine Department-Adan Hospital, Kuwait for their contribution and collaboration in this research.

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