From Hyperthyroidism to Hypothyroidism: A Detailed Analysis of Radioactive Iodine Therapy Outcomes Based on Dosage

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Abstract:

Background: Hyperthyroidism, a common thyroid disorder, is often managed with radioactive iodine (RAI) therapy. However, the efficacy and outcomes of different RAI doses over time remain incompletely understood. This study aimed to evaluate the impact of various RAI doses on thyroid function in hyperthyroidism patients, assessing changes over a 12-month period post-therapy.

Patients and Methods: We conducted a retrospective analysis of 303 hyperthyroidism patients who underwent RAI therapy at two medical centers. Patients were predominantly female (54.8%) with a median age of 38 years. We analyzed thyroid function at 6 and 12 months post-therapy, correlating outcomes with RAI doses ranging from 10-20 mCi. Symptoms, hormone levels, and the presence of anti-TPO antibodies were also assessed.

Results: At 6 months post-RAI, 53.5% of patients developed hypothyroidism, 27.0% were euthyroid, and 19.5% remained hyperthyroid. By 12 months, 79.5% had hypothyroidism. The incidence of hypothyroidism varied with RAI dose, being highest in the 18-20 mCi group. Notably, a dose-dependent response was observed, with higher RAI doses more likely to result in hypothyroidism.

Conclusions: Most Graves' disease patients developed hypothyroidism within one year following RAI131 treatment, with higher doses associated with earlier onset hypothyroidism. RAI131 dosage and other parameters may predict hypothyroidism timing and help guide therapy individualization.

Key words: Graves' disease, radioactive iodine therapy, Hypothyroidism.

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Introduction:

Graves' disease is an autoimmune disorder and common cause of hyperthyroidism, with thyroid-stimulating immunoglobulins activating the thyroid-stimulating hormone receptor, leading to excessive thyroid hormone production and release [1]. Mainstay treatment options for Graves' hyperthyroidism include antithyroid drugs, radioactive iodine-131 (RAI131) therapy, and thyroidectomy. RAI131 is often preferred for its efficacy and safety profile. The radioisotope accumulates in and subsequently destroys parts of the hyperfunctioning thyroid tissue via beta decay irradiation, gradually restoring euthyroid or hypothyroid function [2, 3].

A frequent complication following RAI131 treatment is development of overt hypothyroidism over the first year, occurring in approximately 50-80% of Graves' patients depending on the administered dose [4,5].

This retrospective study aimed to evaluate parameters affecting hypothyroidism timing in Graves' disease patients after RAI131.

Patients and Methods:

STUDY DESIGN

This was a retrospective study utilizing medical records of Graves's disease patients who underwent radioactive iodine-131 (RAI131) therapy between 2013 and 2022. Data was collected from two medical centers in Egypt (Clinical Oncology and Nuclear Medicine department–Assuit University Hospital and Nuclear Medicine department–South Egypt Cancer Institute). The study included patients who had information, lab results, imaging, thyroid scanning, RAI131 therapy, and at least one year of follow-up. The goal was to evaluate factors influencing the development of hypothyroidism after RAI131 treatment for Graves's disease.

STUDY PARTICIPANTS

Patients were included who had a definitive diagnosis of Graves' based on clinical evaluation and lab/imaging findings. Patients were excluded if they had other causes of hyperthyroidism, thyroid cancer, prior thyroid surgery, insufficient follow-up or data. This allowed standardized analysis specifically evaluating hypothyroidism timing in Graves' disease patients after RAI131 therapy.

RECORDED DATA

The data recorded included medical history, physical exam, lab tests (FT3, FT4, TSH, anti-TPO), neck ultrasound, thyroid scan with technetium-99m, and quantitative calculation of 99mTc uptake to determine appropriate 131I dose (range 370-740 MBq). Levels of FT3, FT4, TSH were monitored every 2 months post-therapy to assess treatment response.

Some patients received concurrent prednisolone to prevent Graves' ophthalmopathy exacerbation. There was also a strict protocol for patient preparation and radiation protection measures post 131I therapy.

STATISTICAL ANALYSIS

The data were analyzed using SPSS version 27.0. Continuous variables were presented as median (interquartile range, IQR). Categorical variables were summarized as percentages. A P-value less than 0.05 was considered statistically significant.

Results:

We analyzed data from 524 hyperthyroidism patients who received radioactive iodine (RAI) therapy at two medical centers. Our final cohort included 303 eligible patients, mostly female (54.8%), with a median age of 38 years. The most common symptom was weight loss (93.4%); less frequent symptoms were exophthalmos (19.1%) and palpitations (8.9%). Median hormone levels were abnormal, including low TSH (0.01 μIU/mL), elevated FT4 (3.5 ng/dL), and elevated FT3 (6.46 pg/mL). Of those tested, 62.1% (36/58) were positive for anti-TPO antibodies. Most patients (88.8%) had taken antithyroid medications, primarily carbimazole, for a median of one year before RAI. The initial median RAI dose was 12 mCi.

We assessed thyroid function at 6 and 12 months post-therapy. At 6 months, 53.5% had hypothyroidism, 27.0% were euthyroid, and 19.5% still had hyperthyroidism. By 12 months, 79.5% had hypothyroidism, only 7.9% remained euthyroid, and 12.5% continued to have hyperthyroidism.

The analysis of responses over six months revealed that the rate of hypothyroidism, euthyroidism, and persistent hyperthyroidism varied depending on the dosage. The response rates for the 10–12 mCi dose were 47.9% hypothyroid, 28.6% euthyroid, and 23.5% hyperthyroid (p = 0.010). With the 15 mCi dose, the response rates were 67.2% hypothyroid, 20.9% euthyroid, and 11.9% hyperthyroid. The highest dose of 18–20 mCi resulted in a response rate of 68.4% hypothyroid, 31.6% euthyroid, and no cases of hyperthyroidism. By the end of the year (12 months), this pattern continued, but without statistically significant differences between doses. For the 10–12 mCi dose, there was a rate of hypothyroidism of 77.9%, with only small percentages of euthyroidism. (Table 1).

Table (1): Relation between responses of primary type (Graves' disease) to different dose value of 1st radioactive iodine dose

1st radioactive iodine dose		Response						*p value*
		Hypothyroid		Euthyroid		Hyperthyroid		
Demographic								
6 months	10-12 mci	104	47.9%	62	28.6%	51	23.5%	0.010*
	15 mci	45	67.2%	14	20.9%	8	11.9%	
	18-20 mci	13	68.4%	6	31.6%	0	0.0%	
12 months	10-12 mci	169	77.9%	16	7.4%	32	14.7%	0.218
	15 mci	56	83.6%	5	7.5%	6	9.0%	
	18-20 mci	16	84.2%	3	15.8%	0	0.0%	

Discussion:

The utilization of iodine-131 for the management of Graves' disease is on the rise, particularly as a primary treatment option due to its convenient oral administration, affordability, dependability, safety, and remarkable efficacy. The success rates following RAI treatment vary from 80% to 100%, and in certain cases, individuals may need to undergo two or more treatment sessions [6].

According to the results of our study, there was a significant difference in the response of primary type among the three dose groups at 6 months ($p = 0.010$), but not at 12 months ($p = 0.218$). The proportion of hypothyroid patients increased with higher doses, while the proportion of euthyroid and hyperthyroid patients decreased with higher doses. Patients receiving 10-12 mCi had 47.9% hypothyroidism at 6 months compared to 67.2% with 15 mCi.

Similarly, Madu et al., 2022 [7] demonstrated a trend toward higher hypothyroidism with increased 131I dose, with 68.9% hypothyroidism using 550 MBq (standard dose) compared to 75% hypothyroidism with 800 MBq (high dose). Our standard 10-12 mCi dose aligns closely with their 550 MBq standard dose group.

Also, Husseni, 2016 [8] showed a significant difference in hypothyroidism rates based on 131I activity, with 48.3% hypothyroidism in the 555 MBq group versus only 24.8% with 370 MBq ($p<0.001$). Converting doses, their 555 MBq is approximately 15 mCi, very close to our 15 mCi dose group. Our 10-12 mCi range straddles their lower 370 MBq (10 mCi) dose, the hypothyroidism risk was lower with the first low activity dose relative to higher radioiodine doses.

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