

Original Research Article

THE ROLE OF RADIOACTIVE IODINE IN THYROTOXICOSIS PATIENTS

ABSTRACT

Aims: The primary objective of this study is to investigate the treatment of Graves' Disease (GD) with radioactive iodine ($^{131}\text{I-NaI}$), presenting the clinical symptoms suffered from patients, and evaluating the level of triiodothyronine (T3), thyroxine (T4) and thyroid-stimulating hormone (TSH) before and after the therapy procedure.

Study design: This project is considered as a retrospective project, nonrandomized, observational clinical case series. Clinical symptoms produced by GD were stratified according to patients' gender and age, and a comparison between T3, T4 and TSH was done before and after the radioiodine therapy.

Place and Duration of Study: This study was made under supervision of the Department of Nuclear Medicine, King Abdulaziz University Hospital (KAUH) and the Department of Diagnostic Radiology (KAU), Jeddah, KSA, from November 2012 to May 2013.

Methodology: The records of patients with clinical diagnosis of diagnosed that they have Thyrotoxicosis and registered who were registered in the nuclear medicine department during academic year 2012-2013 to perform thyroid scan retrospectively were analyzed. Data from 21 patients were collected before and after the administration of radioiodine therapeutic activity. Thyroid scintigraphy and thyroid functional test (TFT) were conducted to all patients enrolled in the present study.

Results: The most common clinical symptoms produced by GD were tachycardia, weight loss, excessive sweating and tremors. A total of 90% of patients were under anti-thyroid drug medication before taking radioiodine therapy while 10% were not. TFT results showed that 95% of patients presented abnormal thyroid function. Aside from excessive sweating, no significant association between age and clinical symptoms was observed. A significant increase in TSH level and decrease in T3 and T4 was observed at three-months after therapy procedure. Within six months post-therapy, 60% of patients showed clinical symptoms of hypothyroidism, 30% presented TFT results compatible with normal thyroid function, and only 10% showed no response to treatment therapy.

Conclusion: Radioactive iodine is an excellent alternative for GD treatment compared to other therapeutic approaches, presenting less complication than surgery procedure and reverse possibility when patients are treated with anti-thyroid drug medication.

Keywords: Hyperthyroidism, Graves' disease, Thyroid hormone, ~~radioactive~~ Radioactive iodine.

1. INTRODUCTION

Hyperthyroidism is a type of thyrotoxicosis. If T3 or T4 (or both) serum levels increase are elevated (or both), a hypermetabolic clinical syndrome will occur^[1].

The most common cause of hyperthyroidism is Graves' disease (GD). GD is characterized and recognized when the patient's immune system attacks the thyroid gland leading to a overproduction of the thyroxin hormone and resulting in a-increased body's metabolic rate. This condition promotes health problems in vital organs such as to the heart, and to the central nervous, reproductive and human gastrointestinal tract systems. Also there are a

variety of physical and mental effects caused by high level of thyroid hormones in blood circulation^[2]. The most frequent clinical symptoms of thyrotoxicosis are heat intolerance, nervousness, heart palpitations, fatigue and weight loss. Common symptoms also include sinus tachycardia, tremor, hyperreflexia and agitation^[3], being evidenced a correlation between the degree of thyroid hormone excess and the clinical severity^[4].

The thyroid-stimulating hormone (TSH) level is a sensitive indicator of the thyroid status in patients with an intact hypothalamic-pituitary axis. It is rare that the patient to be is thyrotoxic when TSH level is within a standard value. The TSH suppression with elevated free T3, but normal free T4 describes the thyrotoxicosis condition. Subclinical hyperthyroidism is defined by either suppressed TSH or weak presence of normal free thyroid hormones concentration^[5]. Serologic data combined with thyroid imaging and radiotracer thyroid uptake measurements enable accurate diagnosis and appropriate patient treatment^[6].

Treatment options for GD may include anti-thyroid drug medication, surgery, and radioactive iodine (RAI) administration. The last alternative therapy is based on radiation dose given to thyroid gland when the radioactive iodine is disintegrated into thyroid cells. The follicular cells are destroyed by beta particles emitted in this disintegration and consequently a reduction in thyroid volume is observed and a control of thyrotoxicosis occurs^[7].

The primary purpose of this study is to investigate the treatment of GD with radioactive iodine (¹³¹I-Nal), presenting the clinical symptoms suffered from patients, and evaluating the level of T3, T4 and TSH before and after the therapy procedure, as this procedure is the first line of therapy recommended by the American Thyroid Association^[8].

2. METHODS

This study was conducted on nonrandomized and observational clinical cases. The patients enrolled in this study were all diagnosed with thyrotoxicosis and registered in the Nuclear Medicine Department to perform RAI therapy. This study was made under supervision of the Department of Nuclear Medicine, King Abdulaziz University Hospital (KAUH) and the Department of Diagnostic Radiology (KAU), Jeddah, KSA, from November 2012 to May 2013.

Data from 21 patients presenting clinical symptoms of GD and confirmed by medical exams were collected. All patients were submitted to TFT performed before and after RAI therapy. Both male and female patients, with age ranging from 15 to 65-years old, were considered for entering in this study. Before administering the radioiodine therapeutic activity, a thyroid scintigraphy, using either injection of ^{99m}Tc-pertechnetate or ¹²³I-Nal administration, was performed to all patients aiming to confirm the type of thyroid disorder. The clinical symptoms suffered by GD patients were stratified according to patients' age and gender using the results acquired through TFT. Patients who have received previous radioactive iodine for therapy purposes were all excluded from statistic analysis.

Radioactive iodine (¹³¹I-Nal) therapy was applied to all patients who have GD confirmed by thyroid scintigraphy. Therapeutic activities ranged from 555 MBq to 925 MBq, and all of them were given to patients orally, either in liquid or capsule form. Data from TFT acquired from patients before and after therapy were used to evaluate the therapy response when applying RAI therapy.

Blood samples were collected from all **patients** prior therapy and within two and four months after therapeutic procedure aiming to measure TSH, T3 and T4 and helping to evaluate therapeutic response.

The collected data were statistically analyzed using SPSS computational software.

3. RESULTS

From a total of 39 patients collected in the KAU Hospital, only 11 have performed the TFT, while 28 have not entered in this survey. Thyrotoxicosis was confirmed only on 21 patients. The majority of registered data were from patients aged from 25 to 35-years old, corresponding to 42.9% of the total number of patients, with 61.9% of them identified as

75 female patients as shown in Table 1.
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Table 1. Patients' characteristics

Variable		Number of Patients
Age	15 – 25	5 (23.8%)
	25 – 35	9 (42.9%)
	35 – 45	4 (19.0%)
	45 – 55	2 (9.5%)
	55 – 65	1 (4.58%)
Gender	Male	8 (38.1%)
	Female	13 (61.9%)

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 79 From the assessment of the thyroid survey, 90% of the patients were on anti-thyroid drug
 80 medication before taking radioiodine therapy. According to the thyroid survey analysis, 95%
 81 of the patients have abnormal thyroid function (obtained from thyroid scans), while 29%
 82 have a history of thyroid disease. However, 19% of them had an abnormality on computed
 83 tomography (CT), magnetic resonance imaging (MRI) and on ultrasound (US). In fact, 19%
 84 complained of enlarged thyroid gland while 14% of them were on anti-thyroid drug
 85 medication (Figure 1). The most common type of drug was Carbimazole. Patients showed
 86 symptoms such as tachycardia, weight loss, excessive sweating and tremors. Heat
 87 intolerance was more prevalent in female patients, while other clinical symptoms were equal
 88 in both gender groups, as shown in Table 2.
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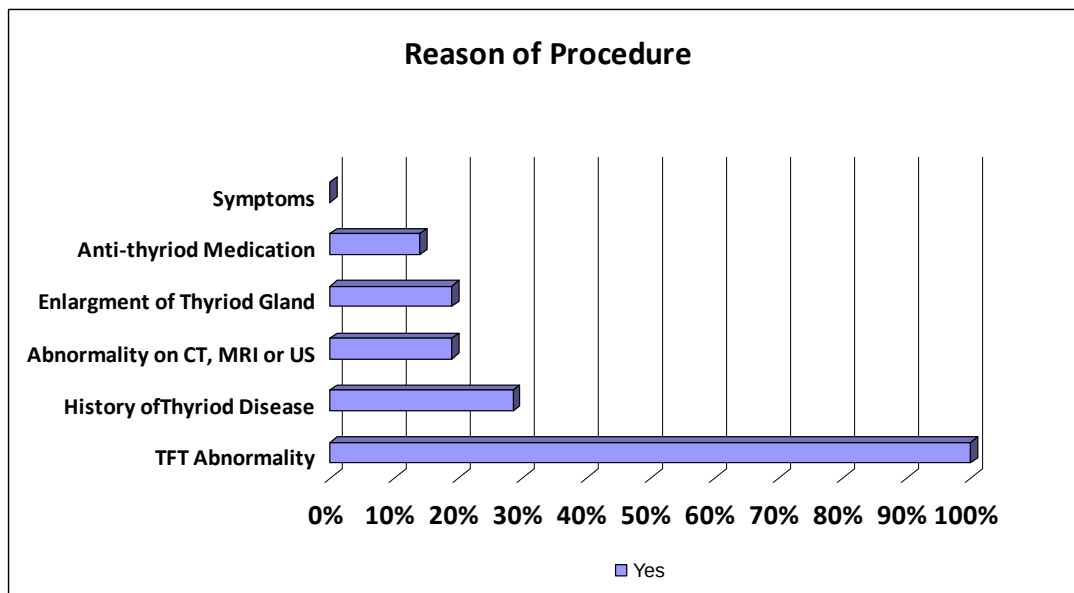


Figure 1. Clinical findings indicating thyroid disorders

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Table 2. Relationship between patients' gender and clinical symptoms

Symptoms		Gender		Uncertainty Coefficient			Test
		Male	Female	Symmetric	Gender	Symptom	
Heat Intolerance	Yes	2	6	0.391	0.383	0.400	Fisher's Exact
	No	12	1				Sig. (0.003*)
Nervousness	Yes	5	11	0.051	0.047	0.057	Fisher's Exact
	No	3	2				Sig. (0.325)
Rapid heart rate	Yes	8	0	0.055	0.035	0.123	Fisher's Exact
	No	12	1				Sig. (1.000)
Weight Loss	Yes	8	0	0.055	0.035	0.123	Fisher's Exact
	No	12	1				Sig. (1.000)
Eyes Changing	Yes	3	5	0.041	0.041	0.040	Chi-Square
	No	8	5				Sig. (0.284)
Excessive sweating	Yes	7	12	0.006	0.005	0.010	Fisher's Exact
	No	1	1				Sig. (1.000)
Tremors	Yes	7	1	0.006	0.005	0.010	Fisher's Exact
	No	12	1				Sig. (1.000)

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100 The Fisher Exact test shows a significant relationship between symptoms and patients' gender (p=0.003). However, most young male patients showed excessive sweating with a significant association (p=0.033). In addition, there are no significant association between age groups and symptoms except for excessive sweating. In excessive sweating, there is a significant relationship between it (p=0.033), and it is a moderate association as it is shown in Table 3. The most common symptoms that have presented a statistical significance were tremors, tachycardia, excessive sweating and weight loss, which correspond to the universal joint clinical symptoms.

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Table 3. Relationship between patients' age and clinical symptoms

Symptoms		Age					Contingency Coefficient	Test
		15 - 25	25 - 35	35 - 45	45 - 55	55 - 65		
Excessive sweating	Yes	5	9	3	2	0	0.608	Fisher's Exact
	No	0	0	1	0	1		Sig. (0.033*)
Nervousness	Yes	4	6	4	2	0	0.458	Fisher's Exact
	No	1	3	0	0	1		Sig. (0.346)
Rapid heart rate	Yes	4	9	4	2	1	0.371	Fisher's Exact
	No	1	0	0	0	0		Sig. (0.571)
Weight Loss	Yes	5	9	3	2	1	0.419	Fisher's Exact
	No	0	0	1	0	0		Sig. (0.333)
Eyes Changing	Yes	3	3	4	1	0	0.476	Fisher's Exact
	No	2	6	0	1	1		Sig. (0.173)
Heat Intolerance	Yes	3	7	4	0	0	0.539	Fisher's Exact
	No	2	2	0	2	1		Sig. (0.073)
Tremors	Yes	4	9	4	1	1	0.469	Fisher's Exact
	No	1	0	0	1	0		Sig. (0.262)

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* 0.0 = No Association, 0.0 < r ≤ 0.2 Very weak, 0.2 < r ≤ 0.4 Weak, 0.4 < r ≤ 0.6 Moderate, 0.6 < r ≤ 0.8 Strong, 0.8 < r ≤ 1.0 Very Strong.

Analysis of the blood samples permitted to verify the significant changes in T3, T4 and TSH levels within three months after radioiodine therapy administration. It was observed a gradual drop in the level of T3 and T4, this last not consistent with therapy response, and at the same time an increase in TSH level. There is a substantial variation among all parameters analyzed, and in other words indicating that radioactive iodine administration produces substantial changes in thyroid functionality and permitting to use this type of therapy as an efficient procedure for cure patients (Table 4).

The correlations between TFT results, acquired before and after treatment, are shown in Table 5. There is a significant relationship between T4 before (T4_B) and after (T4_A) therapy, whilst this relationship between either TSH_B and T3_B or TSH_A and T3_A was considered not statistically significant, this suggesting that the random change in TSH level before and after treatment has no trend. However, it is important to note that TSH level changes in value, before and after therapy.

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Table 4. Descriptive statistics of variation in TSH, T3 and T4 level before and after radioiodine therapy

Variables		Descriptive Statistics		
		Mean	Std. Deviation	Skewness
Before Therapy	TSH_B	0.038	0.172	5.35
	T4_B	39.69	28.21	1.06
	T3_B	16.54	14.44	1.39
After Therapy	TSH_A	16.02	26.61	1.97
	T4_A	15.89	17.17	4.43
	T3_A	5.857	8.567	3.97

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Table 5. Relationship between TSH , T3 and T4 level acquired before and after radioiodine therapy

Comparison	Paired Correlation	
	Correlation	P-Value
TSH_B & TSH_A	-0.088	0.651
T4_B & T4_A	0.357	0.057
T3_B & T3_A	0.486	0.008*

* 0.0 = No Association, 0.0 < r ≤ 0.2 Very weak, 0.2 < r ≤ 0.4 Weak, 0.4 < r ≤ 0.6 Moderate, 0.6 < r ≤ 0.8 Strong, 0.8 < r ≤ 1.0 Very Strong.

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Table 6. Statistical analysis presenting the difference between TSH, T3 and T4 level acquired before and after therapy procedure

Comparison	Paired T-test				
	Mean Differ	95% CI		t	p-Value
TSH_B & TSH_A	-15.98	-26.1	-5.85	-3.23	0.003*
T4_B & T4_A	23.80	13.41	34.18	4.69	0.000*
T3_B & T3_A	10.69	5.851	15.52	4.53	0.000*

* 0.0 = No Association, 0.0 < r ≤ 0.2 Very weak, 0.2 < r ≤ 0.4 Weak, 0.4 < r ≤ 0.6 Moderate, 0.6 < r ≤ 0.8 Strong, 0.8 < r ≤ 1.0 Very Strong.

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One can infer from Table 4 and Table 5 that there is a significant difference between TSH, T3 and T4 values before and after radioiodine therapy, which means that the treatment has a strong effect on thyroid functionality and disease control. However, it was noted that within six months post-therapy administration, 60% of patients were on Thyroxin, indicating a good response to the treatment, 30 % presented standard values of TSH, T3 and T4, and therapy failure was associated to only 10% of patients, this group needing to retake Carbimazole. The degree of response to therapy for all patients can be observed through Figure 32.

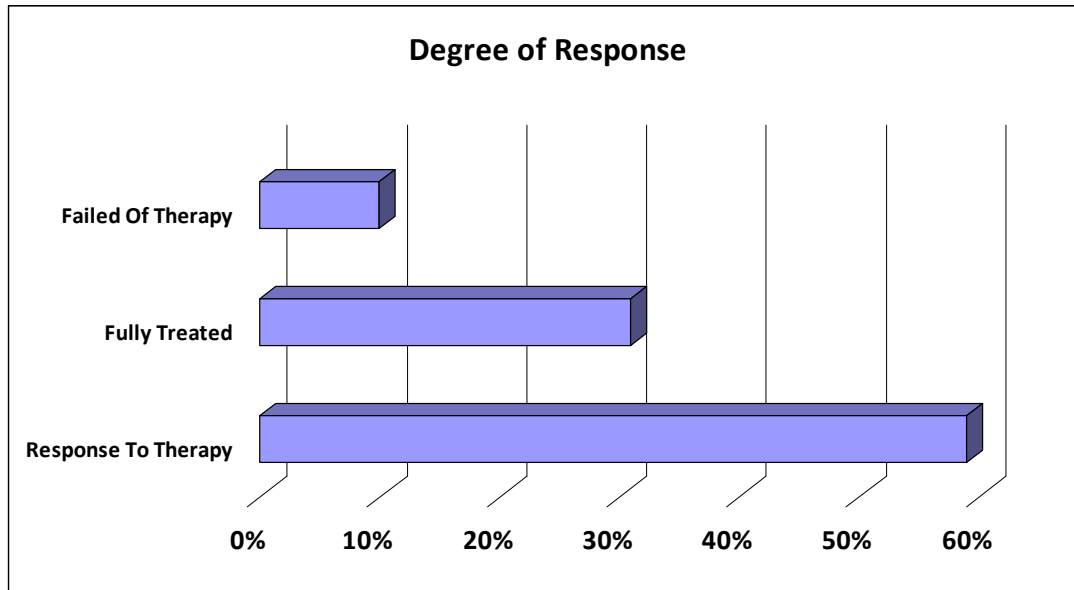


Figure 2. Treatment response experienced by patients after receiving radioiodine therapy for Graves' Disease.

4. DISCUSSION

It was observed in this study that Graves' disease patients responded significantly to the treatment with radioactive iodine. Hypothyroidism was evidenced in 60% of patients and euthyroidism was evidenced in 30% of them within six months after therapy. These results agree with the recommendation of ATA regarding the treatment decision based on thyroid scintigraphy and TFT in order to diagnose thyroid disease more accurately.

Those obtained results were compared with other investigators^[9], where the author describes a retrospective review of more than 450 patients who underwent either radioactive iodine (RAI) therapy (71% of patients) or thyroidectomy (29% of patients) during a six-year period. The percentage of patients who underwent surgery increased significantly over the study period, from 14% to 52%. The authors state that a patient's decision whether to opt for treatment with RAI or surgery usually depends on the presence of clinical manifestations of Graves' disease such as eye disease or goiter. Based on their review of measurements of thyroid-specific autoantibodies for patients with and without ophthalmopathy or goiter, they conclude that the autoantibody measurements are not predictive of these clinical features and, though useful for diagnosis, cannot help patients decide between surgery and RAI.

GD treatment seeks to suppress thyroid function. Options include anti-thyroid drug medication, surgery or radioactive iodine administration (¹³¹I-Nal). Radioiodine is considered a safe and effective therapy with great potential for producing cure rate, although is expected to have a good patient selection and regular follow-up when indicating this therapy^[7].

The purpose of radioiodine therapy is to destroy sufficient thyroid tissue mass to lead the patient to either euthyroidism or hypothyroidism state. There are significant changes in TSH, T3, and T4 values within three months after the administration of ¹³¹I to patients. There is a gradual drop in T3 and T4 values, which is very clear after three months, but not consistent with therapy response. It was noted that TSH level increases in the majority of patients, whilst both T4 and T3 decreases. There is considerable variation among TSH, T3 and T4 values measured before and after radioiodine therapy, and thus indicating that the radioactive iodine has a strong impact on thyroid function.

According to the thyroid survey analysis, 95% of patients have an abnormal thyroid function estimated from thyroid scintigraphy, while only 19% of patients had abnormal on CT, MRI

195 and US. The most common types of clinical symptoms were tachycardia, weight loss,
196 excessive sweating and tremors, compatible with other studies^[10, 11, 12]. The clinical symptom
197 of heat intolerance was more evident in female patient while other symptoms were equal in
198 both gender groups. These results can help physicians to better manage GD patients
199 according to their necessities and respecting their individualities.

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201 **5. CONCLUSION**

202 The present study indicates that radioactive iodine therapy provides excellent treatment for
203 Graves' disease. This alternative therapy is a safe procedure and with lower cost compared
204 to anti-thyroid drug medication and thyroid surgery.

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