

Original Research Article

THE ROLE OF RADIOACTIVE IODINE IN THYROTOXICOSIS PATIENTS

ABSTRACT

Aims: The primary objective is to investigate the Graves' disease (GD) treatment with radioactive iodine ($^{131}\text{I-Nal}$) and correlate the clinical symptoms before and after the therapeutic procedure, while also evaluating T3, T4 and TSH.

Study design: A comparison is done and some factors examined such as age and most common symptoms in hyperthyroidism

Place and Duration of Study: Department of Nuclear Medicine, King Abdulaziz University Hospital (KAUH) and Department of Diagnostic Radiology (KAU), Jeddah, KSA, between Nov. 2012 and May 2013.

Methodology: Data from 39 patients is collected before administration of radioactive iodine dose. Specifically, thyroid scans and Thyroid Function Test (TFT) results are obtained before and after radio-iodine therapy. Patients evaluated within TFT, thyroid survey test to illustrate the demographic feature and response to treatment.

Results: The most common symptoms present are tachycardia, weight loss, excessive sweating and tremors. 90% of patients were on anti-thyroid medication before taking iodine therapy while 10% were not. 95% had abnormal TFT results. Aside from excessive sweating, no significant association between age and symptoms were discovered/observed. Three-months post radio-iodine therapy showed significant increase in Thyroid-Stimulating Hormone (TSH) and decrease of Triiodothyronine (T3) and thyroxine (T4). Within more than six months, 60% of patients showed symptoms of hypothyroidism. 30% of patients being standard and only 10% showed no response to treatment.

Conclusion: Radioactive iodine is an excellent and definitive treatment alternative for GD patients compared to therapy, with less complications in reverse of taking anti-thyroid medication or performing surgery.

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

1. INTRODUCTION

Hyperthyroidism, is a type of thyrotoxicosis. If T3 or T4 serum levels elevate (or both), a hypermetabolic clinical syndrome occurs.^[1]

The most common cause of hyperthyroidism is Graves' disease (GD). GD is characterized and recognized when the immune system attacks the thyroid gland with an overproduction of the thyroxin hormone and an increased metabolic rate. This can lead to a host of health problems involving vital organs such as the heart, central nervous system (CNS), reproductive system and human gastrointestinal tract (GIT) system. The variety of very alarming physical and mental effects caused by this activity.^[2]

GD, followed by toxic multi-nodular goiter, is considered the most common cause of thyrotoxicosis.^[3] The most frequent signs of thyrotoxicosis are heat intolerance, nervousness, heart palpitations, fatigue and weight loss. Common symptoms include sinus tachycardia, tremor, hyperreflexia and agitation.^[3] There is some correlation between the degree of thyroid hormone excess and the clinical severity.^[4]

The exquisitely sensitive indicator of thyroid status in patients with an intact hypothalamic-pituitary axis is called the TSH serum. It is rare that the patient is thyrotoxic when the TSH is

considered normal. The TSH suppression with elevated free T3, but normal free T4 describe thyrotoxicosis. Subclinical hyperthyroidism is defined by suppressed TSH, or weak presence of normal free thyroid hormone concentrations.^[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 medication, surgery and Radioactive Iodine (RAI) therapy. Some patients treated surgically with uncomplicated GD with many choices of treatment that depend on the countries and locations.^[9] The follicular cell destroyed by beta particle and gradually volume decreased and thyrotoxicosis will be controlled.^[15] The primary purpose of this study is to investigate the effect of radioactive iodine therapy on patients who suffer from GD, as it is the first line of therapy recommended by the American Thyroid Association.^[10] Another goal is to measure the sensitivity of thyroid uptake by investigating the condition while giving reasons for hyperthyroidism. Using the static's works, a comparison is done based on confounding factors such as gender, age and most common symptoms in hyperthyroidism.

2. MATERIAL AND METHODS

This study was conducted on nonrandomized, observational clinical cases. The subjects (patients) were all diagnosed with Thyrotoxicosis and are registered in the nuclear medicine department (academic year 2012/2013) to perform thyroid scanned retrospectively analyzed. Data from 39 patients who were subjected to nuclear medicine with symptoms of thyroid disorder and diagnosed with grave's disease was collected. The patients performed a TFT test before and after radioiodine therapy. The exclusion criteria examined in the case of patients who had previous radioiodine treatment doses. Both male and female patients were considered, with an age range between 15 to 65-years old. Before administering the radioactive iodine treatment dose, a thyroid scan was applied to confirm the type of thyroid disorder. The scan clarified the importance and role of radiography scintigraphy in the detection of disease. The patients evaluated using the TFT results to illustrate the demographic feature and response to treatment.

Thyroid Scintigraphy was performed using a radioactive material, which was either ^{99m}Tc injected or ¹²³I swallowed in the form of capsules or liquid.

After obtaining the test results, and Graves' disease was confirmed from the thyroid scan, the treatment ¹²³I was given. Patients are then required perform a blood within two to four months after the treatment is given, and compared with blood test results done prior to the treatment. This will assist in observing the response of the thyroid gland to therapy by measuring TSH, T3 and T4.

Patients were given doses of radioactive iodine orally, either in liquid or capsule form. The range of the doses was between 555 - 925 MBq. The PACS images produced were evaluated. The collected TFT data of each patient in the study before and after the treatment doses is used to evaluate the rate of treatment by using ¹³¹I. The collected data is statistically analyzed using SPSS to investigate the role of radioactive idonine therapy ¹³¹I in the treatment of Graves' disease.

3. RESULTS AND DISCUSSION

3.1 Results

From a total of 39 patients collected in the KAU hospital, only 11 have TFT and thyroid survey results, while 28 did not.

21 patients suffered from Thyrotoxicosis. Data was tested with demographic variables. Mostly, samples were from patients aged between 25 to 35-years old (42.9%), with a majority of them being females (61.9%) as shown in Table 1.

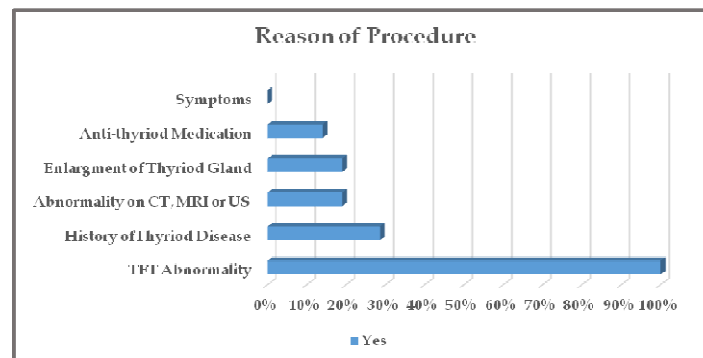
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Table 1. Descriptive Statistics of collected data

Variable		Number %
Age	15 – 25	5 (23.8%)
	25 – 35	9 (42.9%)
	35 – 45	4 (19.0%)
	45 – 55	2 (9.50%)
	55 – 65	1 (4.80%)
	Above 65	0
Gender	Male	8 (38.1%)
	Female	13 (61.9%)

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From the assessment of the thyroid survey, 90% of the patients were on antithyroid medication before taking radioiodine therapy. According to the thyroid survey analysis, 95% of the patients have abnormal thyroid function (obtained from thyroid scans), while 29% have a history of thyroid disease. However, 19% of them had an abnormality on Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Ultrasound (US). In fact, 19% complained of enlarged thyroid gland while 14% of them were on antithyroid medication as it seen from Figure 1. The most common type of medication was Carbimazole. Patients showed symptoms such as tachycardia, weight loss, excessive sweating and tremors. Heat intolerance was more prevalent in female patients, while other symptoms were equal 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. The correlation between gender and each symptoms respectively.

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)

* 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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The Fisher Exact test shows the correlation between gender and the symptoms. The results suggest a strong relationship a 0.003 level of significance.

However, most young male patients showed excessive sweating with a significant association of 0.033. In addition, there are no significant associations between age groups and symptom factors except excessive sweating. In excessive sweating, there is a significant relationship between it (0.604), and it is a moderate association as it seen in Table 3. The most common symptoms that showed significance were tremors, tachycardia, excessive sweating and weight loss, which correspond with universal joint symptoms.

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Table 3. The correlation between Age and each 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.

Thyroid Function Test (TFT)

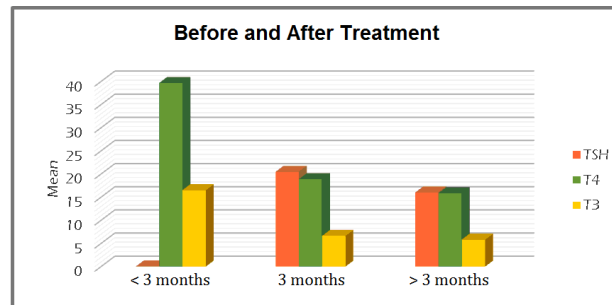
The thyroid gland absorbed the radioactive material within 15-30 minutes of administration when using ^{99m}Tc [9]. The results were collected from 29 patients before and after they dose administration. There is a significant change within three months after the ^{131}I treatment. There is a gradual drop of T4 after three months, inconsistent with responses to therapy. It should be noted that TSH is increased within normal ranges with decreases in both T4 and T3. There is a substantial variation among all parameters, which means that the radioactive iodine response was very high (Table 4 and Figure 2). The relationship between TFT results before and after treatment is shown in Table 5. There is a significant relationship between T4 before (T4_B) and after (T4_A) taking radioactive iodine, and it is increasing but it is not significant between (TSH_B) and (T3_B) before and after (TSH_A) and (T3_A) treatment. The relationship was not significant between test results before and after. These suggest that the random change in TSH before and after treatment has no trend. However, simultaneously, this does not indicate that there is no difference between TSH before and after treatment.

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Table 4. Descriptive statistics of changing the value of TSH, T3 and T4 before and after the treatment

Variables		Descriptive Statistics		
		Mean	Std. Deviation	Skewness
Before	TSH	0.038	0.172	5.35
	T4	39.69	28.21	1.06
	T3	16.54	14.44	1.39
After	TSH	16.02	26.61	1.97
	T4	15.89	17.17	4.43
	T3	5.857	8.567	3.97

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Figure 2. Histogram graph of TSH , T3 and T4 values before and after the treatment

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Table 5. Paired correlation of TSH , T3 and T4 before and after the treatment

Variables	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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It seen in Table 5 that there are significant differences before and after the treatment for TSH, T4 & T3, which means that the treatment has a strong effect on the disease. TSH is seen to increase after treatment whereas T4 & T3 decrease.

However, it is noted that 60% of patients were on Thyroxin; this is an indication of good response to treatment. On the other hand, 30% were normal after treatment and 10% of them encountered failure of therapy by the retaking Carbimazole.

On the other hand, Table 6 shows the relationship between TFT results before and after treatment. It is seen that there is a significant relationship between T4 before and T4 after taking radioactive iodine, and it is increasing but not significant between TSH and T3 before and after treatment. The physiological role of the radioactive iodine (RAI) describes the mechanism of RAI. The iodide transporter of the thyroid takes up the RAI in the similar way as the natural iodine process.

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Table 6. Paired T-test shows the difference before and after the treatment of TSH, T3 and T4

Variables	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.

The relationship between test result before and after was not significant. This suggests that the random change in TSH before and after has no trend. At the same time, this also does not mean that there is no difference in TSH before and after treatment. There are significant differences before and after the treatment for TSH, T4 & T3, which means that the treatment has a high impact on the disease. TSH is increasing after treatment, but T4 & T3 show decrease. However, from Figure 3, 60% of the patients were on Thyroxin, and this is an indication of good response to therapy. On the other hand, 30% were normal after the treatment whereas 10% encountered failure to therapy by the retaking of Carbimazole. The routine thyroid gland imaging due to the high amounts of absorbed radiation doses related to the long physical half-life (eight days) and beta emissions is no longer used. However, ¹³¹I continues to be valuable for the detection of metastases and recurrences in differentiated thyroid cancer.^[16, 17, 18]

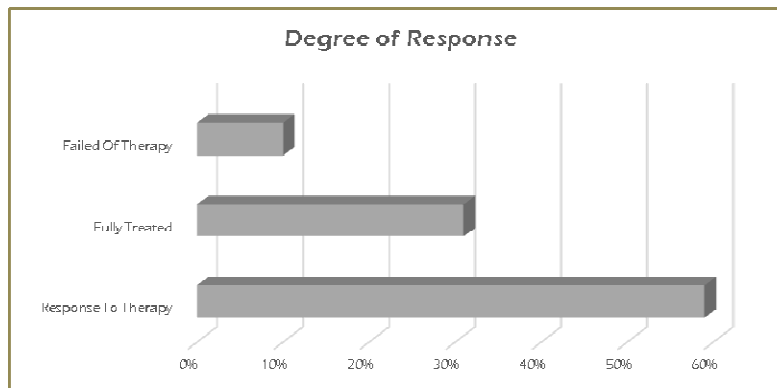


Figure 3. The response to therapy of collected data during the treatment duration.

3.2. Discussion

Graves' disease (GD) is as an autoimmune disorder characterized by the presence of thyroid-stimulating hormone (TSH) receptor antibodies. GD clusters are found in families and genetic relations, but there is no single gene known to be necessary or sufficient to cause GD.^[11, 12] In this study, the from the majority (42.9%) of patients were between 25 to 35-years old , where most were females (61.9%). Assessment of the thyroid survey shows that 90% of the patients were on antithyroid medication before taking radioiodine therapy while 10% were not.^[4] The prevalence of thyrotoxicosis increases with age.^[13, 14]

Graves' disease patients on radioactive iodine therapy responded highly significantly to treatment. 60% of patients developed hypothyroidism, 30% being standard and only 10% did not respond to treatment. This conclusion comes with the recommendation of ATA regarding the treatment decision among this category of patients and shows the importance of performing thyroid scan and TFT in order to diagnose thyroid disease more accurately.

GD treatment seeks to suppress thyroid function. Options include antithyroid medication, surgery or radioactive iodine therapy (¹³¹I). Radioiodine is considered a safe and effective substance with a potentially high cure rate although there are differences for the treatment of thyrotoxicosis with radioactive iodine with proper patient selection and regular follow-up.^[15] Radioactive Iodine (¹³¹I) for Graves' hyperthyroidism has no adverse effects on the health of the patients' offspring.

The purpose of therapy is to destroy sufficient thyroid tissue to help the patient either euthyroid or hypothyroid. It remains the radionuclide choice for treatment because of the long half-life of just over eight days.^[15] In the present study, the radioactive substance was absorbed by the thyroid gland within 15 - 30 minutes of administration, in case of using ^{99m}Tc or 4 - 6 hours using of ¹²³I. These were observed in 29-patients before and after taking the doses. . There is a significant change within three months after taking ¹³¹I the treatment. There is a gradual drop of T4, which is very clear after three months, inconsistent with responses to treatment. It is noted that TSH increases at a normal rate with decreases in both T4 and T3. There is considerable variation among all parameters, which means that the radioactive iodine therapy had a strong impact.

The requirement of high energy collimators results in a reduced spatial resolution. Combined with the fact that the radiation dose delivered is high, this explains why ¹³¹I is unfavorable for thyroid imaging. The two commonly used radiopharmaceuticals for imaging are ¹²³I and technetium-99m pertechnetate as TcO4⁻.^[7, 8]

According to the thyroid survey analysis, 95% of patients have an abnormal thyroid function due to thyroid scan, while 29% have a history of thyroid disease. However, 19% of patients had abnormal on CT, MRI and US, 19% complained of enlarged thyroid glands, while 14% were on antithyroid medication. The most common type of medication was Carbimazole. It can also be noted that most of the patients presented symptoms such as tachycardia, weight loss, excessive sweating and tremors.^[17, 18, 19]

According to these symptoms, the heat intolerance was more in female while other symptoms were equal in both gender groups. Though GD can have adverse effects if left untreated, , it is not typically life threatening. It was found that GD is 5 - 10 times more common in women than in men.^[15]

4. CONCLUSION

The present study indicates that radioactive iodine therapy provides excellent treatment for Graves' disease. It is seen as a safer, lower cost and effective alternative for hyperthyroid patients (with less complication) compared to antithyroid medication or surgery.

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