British Journal of Applied Science & Technology
10(1): 1-7, 2015, Article no.BJAST.15437
ISSN: 2231-0843

SCIENCEDOMAIN *international*
www.sciencedomain.org

The Role of Radioactive Iodine in Thyrotoxicosis Patients

B. Z. Shakhreet[1*], M. Q. Alzawad[1], N. A. Batawil[2,3], S. D. Jastaniah[1], K. G. Alsafi[2,3], H. Y. Abbas[1], S. K. Hagi[3] and M. A. Khafaji[3]

[1]Department of Diagnostic Radiology, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia.
[2]Department of Nuclear Medicine, King Abdulaziz University Hospital, Jeddah, Saudi Arabia.
[3]Department of Radiology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.

Authors' contributions

This work was carried out in collaboration between all authors. Authors BZS and MQA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript and managed literature searches. Authors SDJ, NAB, KGA, SKH and MAK managed the analyses of the study and literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJAST/2015/15437
Editor(s):
(1) A. A. Hanafi-Bojd, Department of Medical Entomology & Vector Control, School of Public Health, Tehran University of Medical Sciences, Iran.
(2) Meng Ma, Anhui University, Hefei, Anhui, China, and Icahn Institute for Genomics and Multiscale Biology, Icahn School of Medicine at Mount Sinai, New York, USA.
Reviewers:
(1) Jeff Fisher, Division of Biochemical Toxicology, US Food and Drug Administration, USA.
(2) Anonymous, Wright State University, USA.
(3) Anonymous, University of São Paulo, Brazil.
(4) Anonymous, Oncology Institute of Vojvodina, Serbia.
(5) Anonymous, University of Cape Town, South Africa.
Complete Peer review History: http://sciencedomain.org/review-history/9749

Original Research Article

Received 25th November 2014
Accepted 5th June 2015
Published 13th June 2015

ABSTRACT

Aims: The primary objective of this study is to investigate the treatment of Graves' Disease (GD) with radioactive iodine (^{131}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, non-randomized, 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.

**Corresponding author: E-mail: bshakhreet@yahoo.com;*

Place and Duration of Study: This study was conducted 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 Thyrotoxicosis who were registered in the nuclear medicine department during academic year 2012-2013 to perform thyroid scan retrospectively were analyzed. Data from 21 patients was collected before and after the administration of radioiodine therapeutic activity. Thyroid scintigraphy and thyroid functional tests (TFT) were conducted on 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 the 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.
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 iodine.

1. INTRODUCTION

Hyperthyroidism is a type of thyrotoxicosis. If T3 or T4 (or both) serum levels increase 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 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 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 the radiation dose given to the 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 (^{131}I-NaI), 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 non-randomized and observational clinical cases. All the patients enrolled in this study were diagnosed with thyrotoxicosis and were 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 exhibiting clinical symptoms of GD, and confirmed by medical exams, were collected. All patients were subjected to TFT, which was performed before and after RAI therapy. Both male and female patients, ranging in age from 15 to 65-years old, were considered for entry into this study. Before administering the radioiodine therapeutic activity, a thyroid scintigraphy, using either an injection of ^{99m}Tc-pertechnetate or ^{123}I-NaI administration, was performed on all patients with the aim 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. Previous patients who had received radioactive iodine for therapy purposes were all excluded from statistical analysis.

Radioactive iodine (^{131}I-NaI) therapy was applied to all patients who had 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, was 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 procedures, with the aim to measure TSH, T3 and T4 and to help 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 only confirmed in 21 patients. The majority of registered data came from patients aged between 25 to 35-years old, corresponding to 42.9% of the total number of patients, with 61.9% of them identified as female patients, as shown in Table 1.

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 (4.8%)
Gender	Male	8 (38.1%)
	Female	13 (61.9%)

From the assessment of the thyroid survey, 90% of the patients were on anti-thyroid drug 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 on ultrasound (US). In fact, 19% complained of enlarged thyroid glands, while 14% of them were on anti-thyroid drug medication (Fig. 1). The most common type of drug was Carbimazole. Patients showed symptoms such as tachycardia, weight loss, excessive sweating and tremors. Heat intolerance was more prevalent in female patients, while other clinical symptoms were equal in both gender groups, as shown in Table 2.

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.

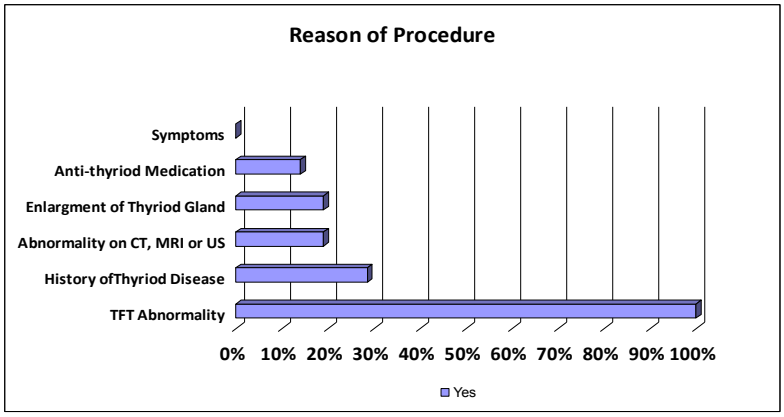

Fig. 1. Clinical findings indicating thyroid disorders

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)

** 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*

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)

** 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 allowed for verification of significant changes in T3, T4 and TSH levels within three months after radioiodine therapy administration. A gradual drop in the levels of T3 and T4 was observed, the latter not consistent with therapy response. At the same time, an increase in TSH levels was observed. There is a substantial variation among all parameters analyzed. In other words, it indicates that radioactive iodine administration produces substantial changes in thyroid functionality and permits for the use of this type of therapy as an efficient procedure for curing 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, thus suggesting that the random change in TSH level before and after treatment has no trend as shown in Table 6. However, it is important to note that TSH level changes in value, before and after therapy.

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 of 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 Fig. 2.

4. DISCUSSION

In this study, it was observed that Graves' disease patients responded significantly to the treatment with radioactive iodine. Within six months after therapy, hypothyroidism was exhibited by 60% of the patients, while euthyroidism was exhibited by 30% of them. 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 auto antibodies 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 (^{131}I-NaI). 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. There are significant changes in TSH, T3, and T4 values within three months after the administration of ^{131}I 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.

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

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 and US. The most common types of clinical symptoms were tachycardia, weight loss, excessive sweating and tremors, compatible with other studies [9,10,11]. The clinical symptom of heat intolerance was more evident in female patient while other symptoms were equal in both gender groups. These results can help physicians to manage GD patients better, according to their necessities and with respect to their individualities.

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.*

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

Comparison	Paired T-test				p-value
	Mean differ	95% CI		t	
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.*

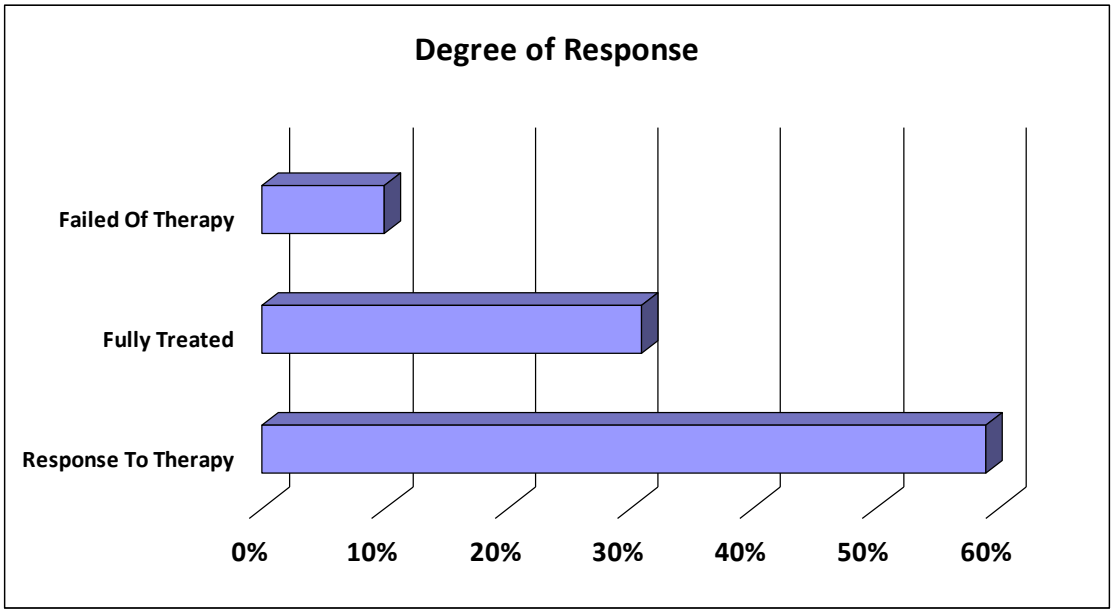

Fig. 2. Treatment response experienced by patients after receiving radioiodine therapy for Graves' disease

5. CONCLUSION

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

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kittisupamongkol W. Hyperthyroidism or thyrotoxicosis? Cleveland Clinic. Journal of Medicine. 2009;76(3):152.
2. Spinas GA, Ott P, Stoeckli SJ. Disorders of the head and neck. In: Siegenthaler W differential diagnosis in internal medicine: From symptom to diagnosis. 1st edn München, Verlag CH Beck. 2007;474-491.
3. Cooper DS. Hyperthyroidism. Lancet. 2003;362:459-68.
4. Boelaert K, Newby PR, Simmonds MJ, Holder RL, Carr-Smith JD, Heward JM, et al. Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med. 2010;123(183e):1–9.
5. Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al. Hyperthyroidism and other causes of thyrotoxicosis: Management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Thyroid. 2011;21:1-54.
6. Pittas AG, Lee SL. Evaluation of thyroid function. In: Hall JE, Nieman LK. Handbook of diagnostic endocrinology. 1st ed. New Jersey; Humana Press. 2003;107-130.
7. Mumtaz M, Lin LS, Hui KC, Mohd Khir AS. Radioiodine I-131 for the therapy of Graves' disease. Malays J Med Sci. 2009; 16(1):25-33.
8. American thyroid association. Hyper-thyroidism management guidelines. Endocrine Practice. 2011;173:2-65.
9. Sarkar SD, Kalapparambath T, Palestro CJ. Comparison of I-123 and I-131 for whole body imaging in thyroid cancer. J Nucl Med. 2002;43:632-634.
10. Sarkar SD, Savitch I. Management of thyroid cancer. Applied Radiol. 2004;34-45.
11. Ward LS, Santarosa PL, Granja F, da Assumpção LV, Savoldi M, Goldman GH. Low expression of sodium iodide symporter identifies aggressive thyroid tumors. Cancer Lett. 2003;200:85-91.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/9749