Predictors of recurrent thyrotoxicosis in a cohort of Egyptian thyrotoxic patients treated with radioactive iodine

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Background
The use of radioactive iodine (RAI) in the treatment of thyrotoxicosis is increasing either in recurrent cases or as first-line therapy. RAI has the advantages of being relatively inexpensive, reliable, safe, easy to administer, and highly effective.
Objective
The purpose of this retrospective study is to assess the efficacy of RAI in the treatment of hyperthyroidism and to determine the different prognostic factors that affect the outcome.
Patients and methods
Our cohort include 60 patients with hyperthyroidism who were treated with RAI in the Nuclear Medicine Unit, Mansoura University Hospital and Internal Medicine Hospital during the period from 2009 to 2015 inclusive. Patients' records were reviewed for the following data: age, gender, history of antithyroid medications (antithyroid drugs), size of the gland, cause of hyperthyroidism (Graves' disease, and multiple and single functioning nodules), level of fT4, and dose of RAI.
Results
There was female predominance of hyperthyroidism with a female to male ratio of 4.5 : 1. Sixty percent of patients were less than or equal to 50 years and 71.7% received antithyroid medications. Thyroid gland was moderately or markedly enlarged in 55% of patients. A high level of fT4 ($>$4 ng/ml) was recorded in 56.7%. Graves' disease was the most common pathological diagnosis. Most patients (68.3%) received a higher dose of RAI ($\geq$10 mCi). After 6 months of RAI therapy; hypothyroidism was observed in 29 patients (48.3%) while 12 were euthyroid (20%). Hypothyroidism was higher in Graves' disease than other causes of thyrotoxicosis (P=0.04), while patients who have previously received antithyroid medications were less likely to develop it (P=0.04). Response to RAI was significantly higher in those with a low level of fT4 (P=0.03), small size of the gland (P=0.02), and higher dose of RAI (P=0.02). Efficacy of RAI was not dependent on age (P=1) and gender (P=1).
Conclusion
Our results of this study of a cohort patient with thyrotoxicosis demonstrated that the size of the thyroid gland, the dose of RAI, use of antithyroid drugs, the cause of thyrotoxicosis, and the level of fT4 significantly affect the response to RAI, while the age and gender do not. So we should appreciate these factors when planning the treatment of such cases.

Keywords:
radioactive iodine, recurrent thyrotoxicosis, hyperthyroidism

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Introduction

Hyperthyroidism is a common disorder that affects all systems of the body [1]. The etiology of hyperthyroidism include Graves' disease, and multiple and single functioning nodules [2]. There are three treatment options for hyperthyroidism: antithyroid drugs (ATDs), thyroidectomy, and radioactive iodine (RAI). Despite ATDs still being the first-line treatment for hyperthyroidism in some countries, they have several drawbacks [3–6]. They are associated with a high prevalence of adverse side effects especially at a young age [7]. Also, they need prolonged use and are associated with high relapse or low remission rates during or after stoppage [8]. Thyroidectomy is an option whenever there is thyroid gland enlargement causing compression on the structures of the neck or there is suggestion of cancer [9,10]. The use of RAI in the treatment of hyperthyroidism is increasing either in recurrent cases

or as first-line therapy [11]. RAI has the advantages of being relatively inexpensive, reliable, safe, easy to administer, and highly effective [12,13].

The use of RAI aimed to treat hyperthyroidism through the destruction of sufficient thyroid tissue so that the patient became euthyroid or hypothyroid [14].

The purpose of this retrospective study is to assess the efficacy of RAI in the treatment of hyperthyroidism and determine the different prognostic factors that affect the outcome.

Patients and methods

Our cohort includes 60 patients with hyperthyroidism who were treated by RAI in the Nuclear Medicine Unit Mansoura University Hospital and Internal Medicine Hospital during the period from 2009 to 2015 inclusive.

This study was approved by the Medical Ethics Committee.

This is retro-spective study depends on data collection. Patients' records were reviewed for the following data: age, gender, history of ATDs, size of the gland, cause of hyperthyroidism (Graves' disease, and multiple and single functioning nodule), level of fT4 and dose of RAI. The reference value of fT4 was 0.8–1.9 ng/ml. The size of the gland was determined through palpation and thyroid scan finding and was classified as normal (impalpable), mild when it was palpably enlarged, but not visible and moderate or marked enlargement when it was palpable and visible. ATDs was stopped for 1 week before RAI. Also, iodine-containing medications were stopped several weeks before therapy and the patient was on a low-iodine diet for 10 days before the therapy. The patient should be fasted before and 2 h after giving the dose to enhance higher absorption of RAI. The doses of RAI therapy were 10–15 mCi which are the arbitrary doses. The calculated doses are 0.15 mCi/g of estimated thyroid weight corrected for the 24-h thyroid uptake [15]. After receiving the dose, the patients were divided into: (1) euthyroid, disappearance of clinical picture of hyperthyroidism with normal range of T3, T4, and TSH. (2) Hypothyroid, high level of TSH with or without low-serum thyroid hormones. In case of elevated TSH on two occasions 4 weeks apart levothyroxine was started. (3) Resistant, there is persistence of thyrotoxic manifestations and fT3or fT4 remained elevated for 3 months.

The results of thyroid function tests were assessed at 6 weeks, 3, and 12months after the RAI therapy. Successful treatment was considered when the patient became euthyroid or hypothyroid without the ATD therapy after RAI within 6 months of therapy.

Results

The clinical characteristics of the 60 patients included in this study are listed in Table 1. There was female predominance of hyperthyroidism with a female to male ratio of 4.5 : 1. Sixty percent of patients were less than equal to 50 years and 71.7% received antithyroid medications. The thyroid gland was moderately or markedly enlarged in 55% of patients. A high level of fT4 (>4 ng/ml) was recorded in 56.7%. Graves' disease was the most common pathology. Most patients (68.3%) received a higher dose of RAI (≥10 mCi).

After 6 months of RAI therapy, hypothyroidism was observed in 29 patients (48.3%) while 12 were euthyroid (20%). Hypothyroidism was higher in Graves' disease than other causes of hyperthyroidism (P=0.04), while the patients who have previously received antithyroid medications were less likely to develop it (P=0.04). The response to RAI was significantly higher in those with a low level of fT4 (P=0.03), small size of the gland (P=0.02), and higher doses of RAI (P=0.02). Efficacy of RAI was not dependent on age (P=1) and gender (P=1) (Table 2).

Table 1 Clinical characteristic of 60 patients

Characters	*N* (%)
Gender	
Male	11 (18.3)
Female	49 (81.7)
Age (years)	
≤50	36 (60)
>50	24 (40)
Use of antithyroid drugs	
Yes	43 (71.7)
No	17 (28.3)
Size of gland	
Average or mild enlargement	27 (45)
Moderate or marked enlargement	33 (55)
fT4 level (ng/ml)	
<4	26 (43.3)
>4	34 (56.7)
Cause of hyperthyriodism	
Graves'disease	38 (63.3)
Autonomus nodule	9 (15)
Multinodular	13 (21.7)
Dose (mCi)	
<10	19 (31.7)
≥10	41 (68.3)

Table 2 Response rate

Responses	*N* (%)
Hypothyroid	23 (38.3)
Euthyroid	12 (20)
No response (persistent hyperthyroidism)	25 (41.7)

Discussion

The estimated prevalence of hyperthyroidism ranges from 0.1to 0.5% with a higher percentage in women than in men with an annual incidence of 6.3% in women [16,17]. The female to male ratio in our patients was 4.5 : 1.

There is an increased tendency for the use of RAI for the treatment of hyperthyroidism that increases the need to study different predictive factors for response [18].

Variable percentage of response to RAI therapy has been reported in many studies; this response depend on several variables including RAI dose [19–21]. In our study, significantly higher response rate was observed with higher doses (≥10 mCi), which coincided with other studies [22,23]. We found that both small size of the gland and low level of fT4 were independent prognostic factors for response. This is in agreement with some studies that stated that the size of the gland and the level of fT4 are significant factors for response [24,25]. As expected, the response to RAI therapy was better in cases of Graves' disease than in multinodular or solitary toxic nodule. That is similar to other published data [25–27]. Explanation for this could be that the suppressed extranodular thyroid tissue does not concentrate RAI and so is exposed to less radiation and continue its normal function after tissue ablation [28].As regards the outcome of RAI therapy in patients who received antithyroid medications, some authors concluded that previous medications decrease the response, while others did not find that [29–32]. In our patients, previous medications affect the response significantly; this may be due to decreased RAI uptake in the gland when treating thyrotoxicosis with medications. Erem *et al.* [19] have reported that both gender and age did not affect the outcome of RAI therapy which is comparable to our results.

Conclusion

Our results of this study of cohort patients with thyrotoxicosis demonstrated that the size of the thyroid gland, dose of RAI, use of ATDs, cause of thyrotoxicosis, and the level of fT4 are factors that significantly affect response to RAI while age and gender are not. So we should put these factors into consideration when planning the treatment for such cases.

Limitations of the study

The first limitation in our study is the small number of patients, because our study was retrospective and those patients were recruited previously. The second limitation is that we have done our study in our center, Mansoura University Hospital (Diabetes Clinic and Nuclear Medicine Department), Mansoura University instead of being done at a multicenter. These limitations need other future research to complete our work in this issue in different centers with large number of patients.

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Conflicts of interest

There are no conflicts of interest.

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