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Original Article

Outcome of Radioiodine Treatment by Using 4-Hour I-131 Uptake Value for Dose Calculation in Graves' Disease

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Abstract

Objective: To evaluate outcome of radioiodine treatment by using 4-hour I-131 uptake value for calculation therapeutic dose for patients with Graves'disease.

Materials and Methods: We studied 122 Graves' disease patients with hyperthyroidism. The 4-hour ^{131}I uptake was done in each patient, the 24- hour ^{131}I uptake was estimated from the equation: *predicted 24 hr ^{131}I uptake = 36.7764 + 0.518 (4 hr ^{131}I uptake)*. The RAI treatment dose was calculated using the formula based on estimated thyroid size and predicted 24-hour ^{131}I uptake. We determined thyroid status of these patients at 1 year after the treatment.

Results: Ninety - five patients (77.9%) were euthyroidism or hypothyroidism at 1 year after treatment, and Twenty-seven patients (21.1%) had persistent hyperthyroidism. The patients who had persistent hyperthyroidism had larger thyroid gland ($P < 0.001$) and higher 4- hr ^{131}I uptake value ($P = 0.003$). We found the outcome of treatment of our study were similar to the outcome of other studies that used other regimens in the treatment of Graves' disease patients with ^{131}I.

Conclusion: Radioiodine treatment (^{131}I) based on 4- hour ^{131}I uptake is an effective treatment for patients with Graves' disease. This approach is safe, simple and convenience for the patients.

Keyword: Hyperthyroidism, Early I-131 uptake

Introduction

Radioactive iodine (^{131}I) has been used for treatment of hyperthyroidism more than 60 years.[1] Currently, it is the most common treatment for Graves' disease.[2] Radioiodine therapy is generally safe, with only harmless side - effects and having a high cost/benefit ratio.[3] A number of therapeutic dosing regimens have been proposed ranging from those based on high precision dosimetry, to a large or fixed doses of ^{131}I intended to cause euthyroidism or hypothyroidism after ^{131}I treatment.[4] Regarding the dose calculation, the most widely used is to calculate the radioiodine dose in microcuries (μCi) per gram of thyroid tissue. The calculation requires an estimated thyroid weight, the dose to be delivered per gram and 24-hour radioactive iodine uptake (RAIU). This method requires the patient has to come for measurement of RAIU for two days. The inconvenience and expense associated with 2 - day test had led many hospitals to use early uptake (3 to 6 hours) of ^{131}I for calculated therapeutic dose.[5-8] This would permit same day uptake measurement and therapy, thus reducing the cost and inconvenience of 2 - days examination.

The purpose of this prospective study was to assess the outcome of treatment by using 4- hour ^{131}I uptake value in the calculation of the treatment dose of radioactive iodine in Graves' disease patients.

Materials and Methods

Patients

One hundred and twenty - nine patients with Graves' disease were recruited in this study. All patients were diagnosed with Graves' disease based on their clinical findings, including the present of hyperthyroidism and a diffuse goiter without nodule and high level of serum thyroid hormones.

Recorded information included : age at the time of therapy , gender ,thyroid weight by palpitation, radioiodine (^{131}I) uptake at 4 -hour, administered ^{131}I treatment dose. Antithyroid drug was discontinued for at least 7 days before ^{131}I administration.

Methods

All patients (n = 129) were given an oral dose of ^{131}I approximately 20 μCi each orally. Radioactive iodine uptake was then performed after 4 hours using a single probe counting system consisting of sodium iodine crystal and single channel analyzer (Quadra 605, Macintosh Corp.). Then we used an equation : **predicted 24 hr ^{131}I uptake = 36.7764 + 0.518 (4 hr ^{131}I uptake)**, to estimated 24- hour ^{131}I uptake based on measured 4-hour ^{131}I uptake[8]. These predicted 24-hour ^{131}I uptake was then used to calculate the therapeutic doses of ^{131}I to be given to the patient. The therapeutic doses were calculated using the following formula; **^{131}I therapeutic dose (mCi) = 100 μCi/gm X thyroid gland weight (gm) X 1000 / (predicted 24 hr ^{131}I uptake) X 100.** In some patients ,antithyroid medications (PTU, MMI) were restarted at least 5 days following the ^{131}I therapy. No patient had thyroid tenderness or thyroid storm in the first 3 months after the therapy.

Follow up after ^{131}I therapy

The patient treatment outcome was patient's thyroid status within 1 year after ^{131}I therapy. A satisfactory outcome is either stable euthyroidism or permanent hypothyroidism. A euthyroid outcome was defined as normal serum FT_3 or FT_4 and TSH concentrations without any medication at 1 yr. A hypothyroid outcome was defined as biochemical evidence of inadequate thyroid hormone production (elevated serum TSH) requiring long - term thyroid

hormone replacement. Hyperthyroidism was defined as elevated serum FT_3 and suppressed TSH, with or without the patient continued to require antithyroid medication or further ^{131}I treatment.

Statistical analysis

Descriptive statistic data for dermographics were presented as the mean ± SD. Univariable analysis for continuous data used Unpair t tests and for category data used Fisher's exact test. Multivariable analysis used binary logistic regression for predict failure rate outcome. Significance was accepted when P value < 0.05.

Ethic

This study protocol was approved by Ethic Committee of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

Result

Of the 129 patients, we were able to obtain follow - up data for 122 patients (94.57%). Their baseline characteristics were shown in Table 1. The average age was 37.5 yr and the female to male ratio was 5 : 1. Thyroid gland weight average approximately 53 gm, the average 4-hr ^{131}I uptake was 56% and the average predicted 24-hr ^{131}I uptake was 66%. The average therapeutic dose of ^{131}I was 8.1 mCi (300 MBq).

Table 2 shows outcomes of ^{131}I treatment at 1 yr. Ninety - five patients (77.9%) were successfully treated (hypothyroidism or euthyroidism), and 27 (22.1%) remained hyperthyroid at 1 year. Of those successfully treated, over 90% responed to ^{131}I therapy within the first 6 months, as judged by biochemical analysis, symptom improvement and/or no requirements for antithryoid medication; the remainder responded within the first year.

The three factors (gender, thyroid weight and 4-hr ^{131}I uptake) were identified by binary logistic regression as effective factors for the outcome of ^{131}I therapy in these hyperthyroid patients. The adjusted odd ratio for gender was 3.57 (CI = 1.054-12.095), thyroid weight was 1.06 (CI = 1.032-1.090) and 4-hr ^{131}I uptake was 1.031 (CI = 1.001-1.063).

Two patients had transient hypothyroidism followed by recurrent hyperthyroidism (Table 3). These patients had low serum FT_4 and elevated

Table 1 Characteristics of 122 patients

Age (years)	37.5 ± 12.3
Sex	
Males	20 (19.6%)
Females	102 (80.4%)
Thyroid weight (gm) *	53.6 ± 29.7
4 hr ^{131}I uptake (%)	56 ± 18.3
Predicted 24 hr ^{131}I uptake (%) **	66 ± 13.4
Dose ^{131}I treatment (mCi) ***	8.1 ± 3.9

* Evaluated thyroid weight by palpation

** Calculated from an equation : predicted 24 hr ^{131}I uptake = 36.7764 + 0.518 (4 hr ^{131}I uptake)

*** Calcualted using the formula : Dose ^{131}I treatment (mCi) = 100 μCi/gm X thyroid weight (gm) X 1.000 / (predicted 24 hr ^{131}I uptake) X 100

serum TSH concentration at 3 months after the ^{131}I therapy in the absence of antithyroid drug. Then they had a spontaneous recurrent thyrotoxicosis at 6 months after the ^{131}I therapy.

Characteristics of patients with persistent hyperthyroidism:

Compared with the patients treated successfully, the patients who has persistent hyperthyroidism were male, had larger thyroid size, higher 4-hr and predicted 24-hr ^{131}I uptake value and higher dose of ^{131}I treatment. The age was the same in both groups.

Discussion

The effectiveness of ^{131}I treatment depends on multiple factors including iodine uptake, effective half - life of the iodine in the gland, distribution of radioactivity within tissue and radio - sensitivity of follicular cells. Five approaches for therapeutic dose calculation for patients with Graves' disease have been employed.[9]

Table 2 Outcome of ^{131}I treatment at 1 yr (n = 122 patients)

	Successful treatment n=95 (77.9%)	Treatment failure n=27 (22.1%)	P value
Age (years)	37.3 ± 11.9	38.2 ± 13.6	0.747
Gender (female/male)	7.6/1	1/1	0.015
Thyroid weight (gm) *	45.4 ± 16.5	82.7 ± 44.7	<0.001
4 hr. ^{131}I uptake (%)	53 .5 ± 17.5	65.3 ± 18.8	0.003
Predicted 24 hr ^{131}I uptake (%) **	64.7 ± 9.2	70.6 ± 9.8	0.005
Dose ^{131}I treatment (mCi) ***	7.1 ± 2.2	11.8 ± 6.0	0.001

* Evaluated thyroid weight by palpation

** Calculated from an equation: predicted 24 hr ^{131}I uptake = 36.7764 + 0.518 (4 hr ^{131}I uptake)

*** Calcualted using the formula: Dose ^{131}I treatment (mCi) = 100 μCi/gm X thyroid weight (gm) X 1000 / (predicted 24 hr ^{131}I uptake) X 100

Table 3 Baseline characteristics, ^{131}I uptake ,treatment dose and serum thyroid hormones after ^{131}I treatment in two patients who had transient hypothyroidism

	Patient No.1	Patient No.2
Gender (female or male)	female	male
Age at treatment (yr)	32	54
Thyroid weight (gm)	70	85
4 hr ^{131}I uptake (%)	54	71
Predicted 24 hr ^{131}I uptake (%)	65	74
Dose ^{131}I treatment (mCi)	10	12
Serum TSH at 3 months after ^{131}I treatment	24	70
Serum FT4 at 3 months after ^{131}I treatment	0.7	0.1

1. small doses repeated as necessary;
2. a large ablative dose;
3. a "sliding scale" based on thyroid size;
4. a standard formula for administered dose based on estimated thyroid size;
5. precise dosimetry for the administered dose.

The most common method in dose determination employs a formula based on estimated thyroid size and 24 -hour RAIU as used in this study.

Hayes AA et al.[6] studied a group of 27 hyperthyroid patients with Graves' disease using a logarithmic regression equation which was developed to predict 24- hour ^{131}I uptake from the 4-hour ^{131}I uptake[5]. They obtained a high correlation between the predicted 24-hour ^{131}I uptake (PUp) and the actual 24-hour ^{131}I uptake ($r = 0.94$). Hennessy JV et al. also studied a group of 51 hyperthyroid patients with Graves' disease using early ^{131}I uptake and reported that the predicted 24-hour ^{131}I uptake correlated well with the actual 24-hour ^{131}I uptake ($r = 0.73$) and the correlation of calculated doses obtaining from the predicted and the actual 24-hour ^{131}I uptake were highly significant ($r = 0.91$).

According to our former study conducted in a group of 160 Graves' disease patients[8], we found high correlation between the predicted 24- hour ^{131}I uptake and the actual 24-hour ^{131}I uptake ($r = 0.73$); the correlation between therapeutic doses based on the predicted 24-hour ^{131}I uptake and the actual 24- hour ^{131}I uptake is 0.92.

In this study, we established the outcome of ^{131}I treatment by using 4-hour ^{131}I uptake value in the calculation of the treatment dose. We concluded that the goal of therapy is euthyroidism or hypothyroidism within 1 year of therapy. Our results show the efficacy of this protocol, at 1 year after treatment we found 77.9% of Graves' disease patients have successful treatment. These results were similar to the other studies that were performed to evaluate the effectiveness of ^{131}I therapy by used the actual 24-hr ^{131}I uptake to calculate the treatment dose.[10-12]

We found that patients with persisted hyperthyroidism had a larger thyroid gland, higher 4-hor and predicted 24-hour ^{131}I uptake value, compared to those who became hypothyroidism or euthyroidism. Two patients (1.6%) had transient hypothyroidism followed by recurrent hyperthyroidism. Other studies have reported similar findings in 1-6% of patients treated with radioactive iodine had transient hypothyroidism.[13-15]

In summary, ^{131}I therapy based on 4-hour radioiodine uptake is an effective treatment for patients with Graves' hyperthyroidism. The advantage of this method is that the uptake and ^{131}I therapy can be performed within the same day; therefore, it is convenience, simple and safe for the patients.

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