# Outcome of Fixed and Uncalculated Dose of Radioiodine in the Treatment of Hyper Functioning Thyroid Nodules

Morteza Taghavi, MD<sup>1</sup> and Hatami Ghazal, MD<sup>2</sup>

<sup>1</sup>Assistant Professor of Endocrinology, Endocrine Research Center Mashhad Medical University, Ahmad Abad Street, Ghaem Hospital, Mashhad, Iran

> <sup>2</sup>Hatami Ghazal, MD Ahmad Abad Street, Ghaem Hospital, Mashhad, Iran

Corresponding author: Morteza Taghavi, MD Assistant Professor of Endocrinology, Endocrine Research Center Mashhad Medical University, Ahmad Abad Street, Ghaem Hospital, Mashhad, Iran Phone: 00989155164037 Fax: 00985118406757 mortezataghavi2003@yahoo.com and taghaviMR@mums.ac.ir

Received: August 10, 2010 Accepted: August 15, 2010

**Abstract.** Introduction: This is a prospective study of patients treated for a solitary toxic nodule with a fixed dose of radioiodine (<sup>131</sup>I) and followed for at least 1 year in Mashhad, north east of Iran. **Methods**: We evaluated 780 patients who presented to the university hospital of Ghaem during a 7-year period because they had at least one thyroid nodule. We found hot thyroid nodules in 95 (12%) patients. Of these patients, 86 (90.5%) were female and 9 (9.5%) were male. Sixty-nine (72.6%) of the patients had thyrotoxicosis and 26 (27.4%) were euthyroid. We treated 49 thyrotoxic patients with <sup>131</sup>I and followed them for a minimum of 12 months. The <sup>131</sup>I dose for all patients was 15 mCi. The patients underwent thyroid function testing before treatment, at 6 months after treatment, and, thereafter, once every year. **Results**: The single fix dose (15 mCi) of radioiodine was sufficient to control hyperthyroidism in most patients (46/49, 93.8%) in 6 months. Because of persistent hyperthyroidism 6 months after the first dose, 3 patients (6.2%) required a second dose. **Conclusion**: A cure rate of 93.8% can occur within 6 months with a fixed and uncalculated dose of radioiodine. This result is similar to the results of treatment with calculated dose of radioiodine.

Keywords Hot thyroid nodule • Radioiodine • Thyrotoxicosis

## Introduction

Thyroid tissue nodularity is common. In the large Framingham, MA study, clinically apparent thyroid nodules were present in 6.4% of women and 1.5% of men.<sup>[1]</sup> The use of ultrasonography showed that 20% to 76% of women had at least one thyroid nodule.<sup>[2,3]</sup>

Fifteen percent of thyroid nodules are hot. Hot nodules are caused by hyperplasia of thyroid follicular cells whose functional capacity is independent of regulation by TSH. Activation of somatic mutations of the TSH-receptor gene or Gs-alpha protein<sup>[4,5]</sup> have been found in toxic adenoma; but mutations of the TSH-receptor gene are the most common cause.<sup>[6-10]</sup>

Radioiodine (<sup>131</sup>I) is widely and successfully used for therapy of patients with toxic adenomas.<sup>[11]</sup> The aim of this study was two-fold: (1) to evaluate the incidence of and acquire demographic data on patients with hot thyroid nodules in Mashhad, north east of Iran; (2) to determine the outcome for patients treated with a fixed dose of radioiodine therapy.

# **Materials and Methods**

During 7 years (May 2002 to April 2009), 780 patients with thyroid nodules presented to the university hospital of Ghaem and were evaluated. Hot thyroid nodules were found in 95 (12%) of the patients.

The diagnosis of a hot nodule was based two factors: (1) the patient had a palpable thyroid nodule corresponding to an area of increased radioiodine concentration on 99mTc-pertechnetate scintigraphy, and (2) suppressed radioiodine uptake in surrounding and contralateral parts of the gland. The diagnosis of hyperthyroidism was based on the clinical picture and thyroid function testing. Overt hyperthyroidism is defined as a suppressed TSH with high thyroid hormones levels; subclinical hyperthyroidism is defined as a suppressed TSH with normal thyroid hormone levels.

The 49 thyrotoxic patients treated with <sup>131</sup>I were followed for a minimum of 12 months. The <sup>131</sup>I dose for all patients was 15 mCi. Thyroid function tests were performed before <sup>131</sup>I treatment, 6 months after treatment, and, thereafter, once every year.

**Statistical Evaluation**: Quantitative data were presented as mean  $\pm$  SD. For statistical evaluation, the Mann-Whitney test and chi-square were used. The level of significance was chosen as P < 0.05.

#### Results

Studies were conducted of 780 patients who had thyroid nodules. Of the 95 patients (12.2%) who had hot thyroid nodules, the mean age was  $44.8 \pm 15.35$ . Of these 95 patients, 86 (90.5%) were female and 9 (9.5%) were male. Sixty-nine (72.6%) of patients had thyrotoxicosis (clinical or subclinical) and 26 (27.4%) were euthyroid (Table 1).

44.8 ± 15.35 Age (years) 86 (90.5%) Males Sex Females 9 (9.5%) Hyperthyroid 69 (72.6%) **Thyroid status** Euthyroid 26 (27.4%) < 4 44 Nodule size (cm) 51  $\geq 4$ 

Table 1. Characteristic of patients.

The mean size of hot nodules was 4.1 centimeters in its largest diameter. Hyperthyroidism at the time of diagnosis was positively correlated with the size of the nodule (P < 0.01).

Radioiodine was given as a single uncalculated dose in 49 patients This single fixed dose (15 mCi) of radioiodine was sufficient to control hyperthyroidism in most of patients (46/49, 93.8%) in 6 months. Due to persistent hyperthyroidism 6 months after the first dose, 3 patients (6.2%) required a second dose. Nobody became hypothyroid during follow-up periods.

No significant differences were seen in the initial thyroid nodule size or thyroid function test results between patients who needed only one <sup>131</sup>I treatment and those who need more than one <sup>131</sup>I treatment.

## Discussion

Toxic adenoma is a common cause of hyperthyroidism. The classic presentation for toxic adenoma is a palpable thyroid nodule. The nodule corresponds to an area of increased radioiodine concentration on thyroid scintigraphy in a hyperthyroid patient.

There are three main ways to treat a toxic adenoma: medical therapy with a thioamides that should continue indefinitely, radioiodine, or surgery.

Radioiodine is widely used for therapy of patients with toxic adenomas and is recognized as a safe and effective treatment.<sup>[11]</sup> It rapidly concentrates in a toxic nodule and causes destruction of the adenoma. Most patients remain euthyroid after radioiodine therapy because the radioiodine mostly accumulates in the hyperfunctioning nodules.<sup>[12]</sup> for complete treatment of thyrotoxicosis, 10% to 20% of patients may need a second or subsequent dose of radioiodine.

In a large study of 364 patients with hot nodules treated with calculated dose of radioiodine due to nodule size and RAIU, similar results were obtained. A single <sup>131</sup>I administration was sufficient to control overt or subclinical hyperthyroidism in 94% of patients.<sup>[13]</sup>

Other studies have included 53, 45, 52, 27, and 62 patients with hot thyroid nodules. Calculated doses of radioiodine was effective in 75% (14), 93 % (15), 98% (16), 93% (17), and 86% (18) of cases.

In the present study, we analyzed the outcome of 49 patients with hyperfunctioning thyroid nodules treated with 15 mCi<sup>131</sup>I at our university hospital during 7 years. We show the effectiveness of an uncalculated fixed dose of radioiodine to treat subclinical or overt hyperthyroidism in 93.8% of our patients. Only 3 patients (6.2%) required a second dose for complete cure of their thyrotoxicosis. Thyroid status and the nodule size did not correlate with the outcome of <sup>131</sup>I therapy, as observed by others.<sup>[19,20]</sup>

## Conclusion

Radioiodine is an effective treatment of thyroid hot nodules even with a fixed and uncalculated dose. A cure rate of 93.8% can occur within 6 months. This result is similar to the results of treatment with calculated doses of radioiodine.

**Acknowledgement:** This study was supported by grants from Mashhad Medical University.

# References

- 1. Vander, J.B., Gaston, E.A., and Dawber, T.R.: The significance of nontoxic thyroid nodules. Final report of a 15-year study of the incidence of thyroid malignancy. *Ann. Intern. Med.*, 69:537,1968.
- Ezzat, S., Sarti, D.A., Cain, D.R., et al.: Thyroid incidentalomas. Prevalence by palpation and ultrasonography. *Arch. Intern. Med.*, 154:1838, 1994.
- Brander, A., Viikinkoski, P., Nickels, J., et al.: Thyroid gland: US screening in a random adult population. *Radiology*, 181:683, 1991.
- Porcellini, A., Ruggiano, G., Pannain, S., et al.: Mutations of thyrotropin receptor isolated from thyroid autonomous functioning adenomas confer TSHindependent growth to thyroid cells. *Oncogene*, 15:781, 1997.
- Parma, J., Duprez, L., Van Sande, J., et al.: Somatic mutations in the thyrotropin receptor gene cause hyperfunctioning thyroid adenomas. *Nature*, 365:649-651, 1993.
- Paschke, R., Tonacchera, M., Van Sande, J., et al.: Identification and functional characterization of two new somatic mutations causing constitutive activation of the thyrotropin receptor in hyperfunctioning autonomous adenomas of the thyroid. J. Clin. Endocrinol. Metab., 79:1785, 1994.
- 7. Porcellini, A., Ciullo, I., Laviola, L., et al.: Novel mutations of thyrotropin receptor gene in thyroid hyperfunctioning adenomas: rapid identification by fine needle aspiration biopsy. *J. Clin. Endocrinol. Metab.*, 79:657, 1994.
- Russo, D., Arturi, F., Wicker, R., et al.: Genetic alterations in thyroid hyperfunctioning adenomas. *J. Clin. Endocrinol. Metab.*, 80:1347, 1995.
- Russo, D., Arturi, F., Suarez, H., et al.: Thyrotropin receptor gene alterations in thyroid hyperfunctioning adenomas. *J. Clin. Endocrinol. Metab.*, 81:1548-1551, 1996.
- Fuhrer, D., Holzapfel, E.P., Wonerow, P., et al. Somatic mutations in the thyrotropin receptor gene and not in the Gsa protein gene in 31 toxic thyroid

nodules. J. Clin. Endocrinol. Metab., 82:3885, 1997.

- 11. Franklyn, J.A.: The management of hyperthyroidism. *N. Engl. J. Med.*, 330:1731, 1994.
- Ross, D.S., Ridgway, E.C., and Daniels, G.H.: Successful treatment of solitary toxic thyroid nodules with relatively low-dose iodine-131, with low prevalence of hypothyroidism. *Ann. Intern. Med.*, 101(4):488-490, 1984.
- Goldstein, R. And Hart, I.R.: Follow-up of solitary autonomous thyroid nodules treated with <sup>131</sup>I. N. Engl. J. Med., 309:1477–1480, 1983.
- Nygaard, B.: Changes in thyroid technetium-99m scintigram after antithyroid and subsequent radioiodine treatment for solitary autonomous nodule. *Thyroid*, 8: 223–227, 1998.
- Ross, D.S., Ridgway, E.C., and Daniels, G.H.: Successful treatment of solitary toxic thyroid nodules with relatively low-dose iodine-131, with low prevalence of hypothyroidism. *Ann. Intern. Med.*, 101(4):488-490, 1984.
- Huysmans, D.A., Corstens, F.H., and Kloppenborg, P.W.: Long-term follow-up in toxic solitary autonomous thyroid nodules treated with radioactive iodine. J. Nucl. Med., 32(1):27-30. 1991.
- Hegedüs, L., Veiergang, D., Karstrup, S., et al.:
  <sup>131</sup>I-therapy of solitary autonomous thyroid nodules: effect on thyroid size and early hypothyroidism. *Acta. Endocrinol.* (Copenh), 113(2):226-232, 1986.
- Nygaard, B., Hegedüs, L., Nielsen, K.G., et al.: Long-term effect of radioactive iodine on thyroid function and size in patients with solitary autonomously functioning toxic thyroid nodules. *Clin. Endocrinol.* (Oxf), 50(2):197-2021, 1999.
- Ceccarelli, C., Bencivelli, W., Vitti P., et al.: Outcome of radioiodine-131 therapy in hyperfunctioning thyroid nodules: a 20 years' retrospective study. *Clin. Endocrinol.*, 62 (3):331-335, 2005.
- Nygaard, B., Hegedüs, L., Nielsen, K.G., et al.: Long-term effect of radioactive iodine on thyroid function and size in patients with solitary autonomously functioning toxic thyroid nodules. *Clin. Endocrinol.*, 50 (2) :197-202, 2001.