

Is it safe to treat hyperthyroid patients with I-131 without fear of thyroid storm?

Vani VIJAYAKUMAR, M.L. NUSYNOWITZ and S. ALI

Section of Nuclear Medicine, Department of Radiology, The University of Texas Medical Branch, Galveston, USA

Objectives: Thyroid storm is extremely rare. However, hyperthyroid patients with severe thyrotoxicosis are frequently not treated immediately with I-131 for fear of thyroid storm but are placed on thiouracil drugs for varying periods of time. We demonstrate herein that it is safe to treat these patients with I-131, without pretreatment with thiouracil drugs, provided they do not have complicating intercurrent disease. Our definition of severe hyperthyroidism includes marked signs and symptoms of thyrotoxicosis, suppressed TSH, markedly elevated free T4 and/or free T3 and elevated radioactive iodine uptake (RAIU) (>30%) at 4 or 24 hours. Our diagnostic criteria for thyroid storm include two or more findings of fever (>38°C, 100°F), severe tachycardia, high pulse pressure, agitation with tremors, flushing, sweating, heart failure, nausea, vomiting, diarrhea, jaundice associated with high free T4 and/or free T3. **Methods:** Patients were selected retrospectively for the period between August 2003 and December 2004. One hundred and twenty-two patient visits were identified. These patients were treated with 370–740 MBq (10–20 mCi) of I-131 and were evaluated for any evidence of thyroid storm. Most of the patients were placed on beta blocker drugs at the time of initial I-131 therapy; these were continued for at least two months, when the first follow-up visit occurred. At the time of I-131 therapy, it is our policy to educate the patients to seek immediate medical attention for exacerbation of symptoms of thyrotoxicosis. **Results:** Not one of these patients developed thyroid storm. A subset of 25% of these cases with higher potential for thyroid storm (RAIU more than 65%, very marked signs and symptoms, and very markedly elevated free T4 and/or free T3) also tolerated the I-131 therapy well with marked clinical improvement and no exacerbation of the thyrotoxic state. **Conclusion:** It is safe to administer I-131 to patients who are severely hyperthyroid without fear of thyroid storm, provided beta blockade drugs are used to control the signs and symptoms; patient education is also important. With these steps, 4–6 weeks of prior medical treatment may not be necessary.

Key words: thyroid storm, I-131, thyrotoxicosis

INTRODUCTION

THYROID STORM (TS) is an acute, life threatening thyroid hormone-induced hypermetabolic state in patients with thyrotoxicosis. It is rare, occurring in 1–2% of hyperthyroid patients.^{1,2} If unrecognized and untreated, it is often fatal with mortality as high as 20%. Other underlying

illnesses often contribute to the cause of death. TS is one of the rare complications of radioiodine therapy for hyperthyroidism with severe thyrotoxicosis.

Radioactive iodine (I-131) therapy for hyperthyroidism is effective and safe,^{3,4} and has been used extensively for more than six decades. However, patients with newly diagnosed hyperthyroidism are often pretreated with antithyroid drugs before I-131 therapy is considered in the belief that antithyroid drugs will deplete thyroid hormonal stores and thus prevent or reduce the risk of radioiodine induced TS³; not enough data are available to support this hypothesis. I-131 therapy has been shown to increase circulating stimulating TSH receptor antibodies

Received October 6, 2005, revision accepted April 4, 2006.

For reprint contact: Vani Vijayakumar, M.D., Director of Nuclear Medicine, Clinical Science Bldg., Rm. 2.474, 301 University Blvd., Galveston, TX 77555-0793, USA.

E-mail: vavijaya@utmb.edu

from dying thyroid cells; these can precipitate thyroid storm. A large proportion of these antibodies are released during the first few weeks after radioiodine administration and hence thyroid storm is most likely to occur during this time. Occasionally TS can occur later.

MATERIALS AND METHODS

This is a retrospective review of hyperthyroid patients seen in our thyroid clinic between August 2003 and December 2004. Patients who had more than 30% radioactive iodine uptake (RAIU) at 4 or 24 hours and who received radioactive iodine (RAI) therapy were selected. A total of 122 patient visits were identified. All the patients had typical signs and symptoms of hyperthyroidism and abnormal thyroid function tests. A pregnancy test was obtained for all the patients of child bearing age. Informed and witnessed consent was obtained from all the patients before RAI treatment. Beta blocking drugs were instituted or continued until a 2-month follow-up visit and longer if necessary. We use larger dosages than frequently employed, often starting patients on 120–160 mg of propranolol or equivalent daily, using pulse rate and blood pressure response to titrate dosage. Education about exacerbation of symptoms and thyroid storm was done during the initial treatment with I-131.

RESULTS

Patient characteristics are summarized in Table 1.

Ninety-two patients had one RAI treatment. Twenty patients had two RAI treatments and 2 patients had three RAI treatments. Eight patients had no RAI treatment. Of those, one patient was trying to get pregnant and wanted to wait and three patients were on Propylthiouracil (PTU). Four patients were thought to be extremely thyrotoxic at the initial visit and were placed on PTU until the thyrotoxic state regressed significantly (6–8 weeks).

Follow-up

On follow up, 12 patients became hypothyroid within two months and 4 patients within 4 months. None of the patients developed thyroid storm. The subgroup of 25% of patients with severe thyrotoxicosis, markedly elevated RAIU, FT4, and low TSH tolerated I-131 therapy well,

with marked clinical improvement during the follow up period. This subgroup of 34 thyrotoxic patients who were treated with I-131 consisted of 25 females and 9 males with ages ranging 14–60 years under the same clinical condition as the four patients who were not treated with I-131. Twenty-two of these patients were pretreated with Propylthiouracil or Methimazole and 12 patients were not pretreated with any thiouracil drugs. All these patients including the 12 patients who were not pretreated with thiouracil drugs tolerated I-131 therapy well without developing thyroid storm.

DISCUSSION

Hyperthyroidism is a common endocrine condition. RAI therapy is the most commonly used modality to treat hyperthyroidism and is indeed in most cases, the treatment of choice. Occurrence of thyroid storm after RAI therapy is extremely rare.^{5–7} Other underlying illnesses often contribute to precipitate thyroid storm.

Diagnosis of thyroid storm is mostly based on clinical findings as the degree of abnormality of laboratory thyroid function tests can not differentiate thyrotoxicosis and thyroid storm. The findings of thyroid storm include fever (>38°C, 100°F), flushing, sweating, severe tachycardia often with atrial fibrillation, high pulse pressure, occasional heart failure, agitation, delirium, coma, nausea, vomiting, diarrhea, and jaundice.⁸

Hyperthyroidism presents in a number of different forms, the three most common being Graves' disease, Toxic multinodular goiter and Hyperfunctioning follicular Adenoma. Graves' disease is by far the most common form of overt hyperthyroidism, with known immunologic etiology. Classic findings of Graves' hyperthyroidism include goiter, exophthalmos, and pretibial myxedema. Thyroid storm usually occurs in patients with known hyperthyroidism and is not common during the first four years after the initial diagnosis.⁹

Up to one half of patients presenting to the emergency department in thyroid storm report a dramatic weight loss of more than 40 lbs. Other presenting symptoms include palpitations, disorientation, tremor, chest pain, emotional lability, nervousness, dyspnea, heat intolerance, psychosis, increased sweating, edema, fatigue, anxiety, weakness and increased appetite.

Precipitating Factors

Thyroid storm can be triggered by several events.^{1,2} Infection, in particular pulmonary infection is a common major precipitating event. Other contributing factors include an autoimmune trigger, diabetic ketoacidosis, hyperosmolar coma, insulin-induced hypoglycemia, attempted surgical treatment of hyperthyroidism, withdrawal of antithyroid medication, radioactive iodine, vigorous palpation of the thyroid gland in hyperthyroid patients, emotional stress, thyroid hormone overdose,

Table 1

Patient characteristics	Range/Number
Age	15–64 years
Sex	M: 46 – F: 76
Diagnosis	Graves': 118, TMNG: 4
TSH	<0.01–0.06 (0.35–5.5)
FT4	0.91– >12 (0.89–1.76)
RAIU	31–94% (<30%)
RAI	7.5–29.9 mCi

cardiovascular events and toxemia of pregnancy.

Diagnosis

The diagnosis is made exclusively by clinical examination. TS occurs predominantly in females, most commonly in women in the third through sixth decades of life. Pre-existing Graves' or toxic multinodular goiter triggers TS. As stated, thyroid function tests do not distinguish thyrotoxicosis from thyroid storm. Occasionally TS can present as multiorgan failure.¹⁰ McCune-Albright syndrome had been associated with thyrotoxic crisis.¹¹

Treatment

Treatment of TS is mostly supportive care. Antipyretics, hydration, supplemental oxygen, antithyroid medications, iodide agents and beta-blockers have been used to alleviate the symptoms.

Response to Treatment

Clinical improvement usually occurs in 24 hours with resolution of crisis in one week. Prompt treatment reduces mortality to less than 20%. The precipitating factor is often the cause of death. TS after RAI treatment is extremely rare and controversial.^{3,12} Rare case reports and few data of thyroid storm associated with other conditions are available.¹³⁻¹⁹ Clinical and biochemical changes after RAI treatment with no clinically significant exacerbations of hyperthyroidism have been reported.^{3,4,7} The need for pretreatment with antithyroid medications is controversial. Radioactive iodine induced thyroiditis can also mimic thyroid storm.²⁰ Sometimes it is difficult to differentiate thyroid storm occurring as a result of RAI treatment or withdrawal of antithyroid medication prior to RAI therapy.²¹

CONCLUSION

After the review it is concluded that it may not be necessary to pretreat four of our thyrotoxic patients with PTU. Since thyroid storm after RAI therapy is rare, it is safe to treat hyperthyroid patients with RAI. Simultaneous beta-blockers and patient education are important. Routine 4-6 weeks of prior medical treatment may not be necessary. However, high risk patients, like the elderly, those with underlying illnesses, or severe thyrotoxic symptoms may require pre and post radioiodine thyrostatic medications.

REFERENCES

1. Manifold AC. Hyperthyroidism, Thyroid storm, and Graves' Disease. *E-medicine* 2005; April 4: 1-18.
2. Singhal A, Campbell D. Thyroid Storm. *E-medicine* 2005; March: 1-16.
3. Koomstra JJ, Kerstens MN, Hoving J, Visscher KJ, Schade JH, Gort HB, et al. Clinical and biochemical changes

- following ¹³¹I therapy for hyperthyroidism in patients not pretreated with antithyroid drugs. *Neth J Med* 1999; 55: 215-221.
4. Kreisig T, Abenhardt W, Mann K, Kirsch CM, Moser E. Early changes in thyroid hormones following radioiodine therapy of hyperthyroidism with reference to etiology and accompanying medication. *Klin Wochenscher* 1989; 67: 386-392.
5. McDermott MT, Kidd GS, Dodson LE Jr, Hofeldt FD. Radioiodine-induced thyroid storm. Case report and literature review. *Am J Med* 1983; 75: 353-359.
6. Tony JC, Verghese R, Mathew G. Radio iodine induced thyroid storm. *J assoc Physicians India* 1994; 42: 924-925.
7. Shafer RB, Nuttall FQ. Acute changes in thyroid function in patients treated with radioactive iodine. *Lancet* 1975; 2: 635-637.
8. Greenspan FS. The Thyroid Gland. In: Greenspan FS, Strewler GJ, eds. *Basic & Clinical Endocrinology*. Fifth edition. Stamford; Appleton & Lange, 1997: 238.
9. Malchiodi L. Thyroid storm: recognizing the signs and symptoms of this life-threatening complication. *AJN* 2002; 102: 33-35.
10. Jiang YZ, Hutchinson KA, Bartelloni P, Manthous CA. Thyroid storm presenting as multiple organ dysfunction syndrome. *Chest* 2000; 118: 877-879.
11. Isotani H, Sanda K, Kameoka K, Takamatsu J. McCune-Albright syndrome associated with non-autoimmune type of hyperthyroidism with development of thyrotoxic crisis. *Horm Res* 2000; 53: 256-259.
12. Sheeler LR, Skillern PG, Schumacher OP, Eversman JJ. Radioiodine-induced thyroid storm: a point of controversy. *Am J Med* 198; 76: A98.
13. Nakamura S, Nishmyama T, Hanaoka K. Perioperative thyroid storm in a patient with undiscovered hyperthyroidism. *Masui* 2005; 54: 418-419.
14. Sebe A, Satar S, Sari A. Thyroid storm induced by aspirin intoxication and the effect of hemodialysis: a case report. *Adv Ther* 2004; 21: 173-177.
15. Al-Anazi KA, Inam S, Jeha MT, Judzewitch R. Thyrotoxic crisis induced by cytotoxic chemotherapy. *Support Care Cancer* 2005; 13: 196-198.
16. Ramirez JI, Petrone P, Kuncir EJ, Asensio JA. Thyroid storm induced by strangulation. *South Med J* 2004; 97: 608-610.
17. Jao YT, Chen Y, Lee WH, Tai FT. Thyroid storm and ventricular tachycardia. *South Med J* 2004; 97: 604-607.
18. Waltman PA, Brewer JM, Lobert S. Thyroid storm during pregnancy. A medical emergency. *Crit Care Nurse* 2004; 24: 74-79.
19. Hayek A. Thyroid storm following radioiodine for thyrotoxicosis. *J Pediatr* 1978; 93: 978-980.
20. Zuniga-Gonzalez S. Thyroiditis induced by radioactive iodine (I-131). Report of a case and review of the literature. *Gac Med Mex* 2000; 136: 65-69.
21. Kadmon PM, Noto RB, Boney CM, Goodwin G, Gruppuso PA. Thyroid storm in a child following radioactive iodine (RAI) therapy: a consequence of RAI versus withdrawal of antithyroid medication. *J Clin Endocrinol Metab* 2001; 86: 1865-1867.