

Clinical outcome during the Peri-operative (Thyroidectomy) Period of Severely Hyperthyroid Patients with Normalized Pre-operative Free-T4 Levels: Importance of I-131 Therapy as a part of Pre-operative Preparation

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Abstract

Thyroidectomy is performed for hyperthyroidism on patients who do not respond to or are not compliant with medical therapy and in patients with very large goiters causing compressive symptoms. All thyrotoxic patients undergoing thyroidectomy usually are first treated with anti-thyroid drugs to normalize free thyroid hormone levels and render them euthyroid before surgery in order to prevent complications particularly thyroid storm and circulatory collapse. In this case series, we describe the clinical outcome during the perioperative (thyroidectomy) period of three severely hyperthyroid patients, two females and one male, with ages ranging from 13 to 38 years. All patients had grade III goiter, and only one had exophthalmos. The mean duration of goiter was 3.6 years. All of them were given preoperative treatment consisting of propylthiouracil (PTU) at 450-600 mg/day; iodone, 3 tablets daily and propranolol at 30-120 mg/day for one month. All of them had normalized preoperative thyroid function tests. In addition to the preoperative medications mentioned above, all three patients received radioactive iodine therapy before surgery. The first two patients received relatively low doses of 8.0 and 7.5 mCi of I-131 respectively. Unfortunately the first patient had supraventricular tachycardia (SVT), post skin cutting and the other one went into thyroid storm. The third patient who received a cumulative dose of 23.5 mCi of I-131 before surgery had an uneventful postoperative course. It is concluded that normalization of thyroid hormone parameters, especially free T4 is not sufficient for an uneventful and uncomplicated peri-thyroidectomy period in severely hyperthyroid patients with large goiters. Effective radioactive iodine therapy might prove to be helpful in inducing thyroid tissue fibrosis, thus leading to true clinical euthyroidism and excellent clinical course postoperatively.

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Introduction

Graves' disease is an autoimmune disease characterized by a metabolic imbalance resulting from overproduction of thyroid hormones (thyrotoxicosis). Currently, there are at least three methods of treatment: surgery, radioactive iodine (RAI) and antithyroid drugs (ATD). All these treatment options are directed at the thyroid gland or at the manifestations of excess production of thyroid hormones. Previous studies on the long-term use of anti-thyroid drugs have revealed remission rates of 40-50% after prolonged therapy (1). Generally anti-thyroid drugs, which include thionamide derivatives propylthiouracil (PTU), methimazole (MMI) and carbimazole, are employed to achieve euthyroid state before radioactive iodine or surgery. Thyroidectomy is indicated in cases of allergy or unresponsiveness to anti-thyroid drugs (ATD), large goiters with compressive symptoms and in situations where radioactive iodine is contraindicated as in pregnancy (2). Recent studies have shown a higher recurrence rate of hyperthyroidism after subtotal than total thyroidectomy (10-15% vs. < 3%) (3). Thyroidectomy is associated with complications such as recurrent laryngeal nerve damage, permanent hypoparathyroidism, transient hypocalcaemia and mortality (in < 1% in most centers) (4). In the past, thyroid storm used to occur frequently following surgery, but now-a-days it is usually a complication of the untreated or poorly treated disease, rather than a postoperative complication. Pre-operative control of the thyrotoxic state has reduced this phenomenon (5). Radioactive iodine (I-131) therapy is the treatment of choice for patients who are at poor risk for surgery because of complicating medical conditions (6). Several studies attest to the safety of radioactive iodine therapy in adults. In a survey among patients receiving radioactive iodine to treat hyperthyroidism or thyroid cancer, Hall et al (7) found no significant increase in the incidence of leukemia. The success of radioactive iodine therapy is influenced not only

by the size of the thyroid gland and by circulating levels of the thyroid stimulating antibody but also by the individual variation in the sensitivity of the thyroid to radioactive iodine (8,9). This study is a case series that aims to describe three cases of severely hyperthyroid patients who were subjected to thyroidectomy after having been adequately treated with antithyroid drugs and variable doses of radioactive iodine (I-131). Two out of the three patients, in spite of being bio-chemically euthyroid had complicated perioperative courses. The third case, which was treated with a much larger dose of I-131 as compared to the first two, did not suffer from any perioperative problem, and had an uneventful post-operative recovery.

Patients and Methods

Three patients of hyperthyroidism were subjected to thyroidectomy. Their clinical profiles were as follows:

Patient No.1

R.R. a 38-year old female, Filipino, hyperthyroid for 5 years and maintained on methimazole and propranolol. But despite these medications, patient remained hyperthyroid. She was subsequently treated with 8 mCi of I-131. Four months after the radioactive iodine therapy, patient noted marked improvement of symptoms but she still remained thyrotoxic and had persistent goiter. Another radioactive iodine therapy was contemplated but because of financial constraints, patient opted for thyroidectomy. Preoperative medications consisted of the following: 600 mg propylthiouracil (PTU), 40 mg propranolol and 3 tablets iodone daily for a period of one month prior to surgery. Seven months after the initial consultation, she underwent thyroidectomy. Intraoperatively, upon cutting up the skin, patient developed supra-ventricular tachycardia (SVT). Hence, operation was cancelled and patient eventually received 2 more doses of I-131 therapy (5.7 and 6.0 mCi). Presently, the patient is on levo-thyroxine replacement therapy at 75 µgms per day.

Patient No.2

I.R., a 22-year old female, Filipino, has been hyperthyroid for 4 years with irregular intake of anti-thyroid medications. At first consultation she was started on propylthiouracil (300 mg daily) and propranolol (40 mg/day), which she continued for 6 months. However she continued to be thyrotoxic. Hence she was treated with 7 mCi of I-131. A second dose of I-131 was also contemplated after a few months. But the patient preferred to undergo surgery. As in the first patient, she was also administered preoperative medications consisting of PTU 600 mg, Iodone 3 tablets and propranolol 40mg per day. After a month of preoperative preparation, patient underwent thyroidectomy. Immediately after surgery, patient developed thyroid storm with shock, hypotension and DIC. Patient was subsequently stabilized and

discharged.

Patient No.3

J.M., a 14-year old male, American, has been hyperthyroid for 2 years. Ultrasound of the thyroid gland showed diffusely enlarged thyroid lobes. Within 8 months of anti-thyroid medication and regular follow-up, patient received a total dose 23.5 mCi of I-131. Serial thyroid ultrasounds revealed significant reduction in goiter size following I-131 therapy. In spite of anti-thyroid drugs and I-131 therapy the patient remained clinically hyperthyroid. Hence total thyroidectomy was contemplated after an adequate pre-operative preparation and control of the disease with PTU (600 mg per day), Propranolol (40 mg per day) and Iodone (3 tablets per day) over a period of one month. Postoperative follow-up course was uneventful.

Discussion

The mean age of the three patients who are being presented in this paper was 24 years. All three patients had Grade III goiters, and the mean duration of goiters was 3.6 years. Only one of the three patients had ophthalmopathy. The average TSH level prior to thyroidectomy in the three patients was 0.6 µIU/ml. Patient Nos-1 and 2 received doses of 8.0 and 7.5 mCi of I-131 respectively, while Patient No-3 received a total of 23.5 mCi of I-131 prior to surgery. All patients received daily doses of propranolol 40 mg, PTU 600 mg and Iodone 3 tablets as pre-operative medication. The first two patients who received relatively low doses of I-131 (e.g., 8.0 and 7.5 mCi respectively) developed thyroid storm post-operatively, while the third patient (Patient No-3) who received a much higher dose of I-131 (23.5 mCi) had a unremarkable perioperative and uneventful post-operative course devoid of any medical or surgical complication.

Iodine-131 therapy constitutes the most important aspect in the management of Graves' disease. Normally a dose of 5-15 mCi of I-131 (80-120 µCi/gm of thyroid tissue) is administered depending on the size of the thyroid gland and level of percentage uptake of I-131 by the thyroid gland. Larger thyroid glands (> 80 g) may require higher doses. With such radioiodine dosing, 60% of patients would achieve euthyroid status within 6 months and virtually all patients become euthyroid within a year (10). Several groups from around the world have described numerous methods of dose determination for radioiodine therapy of thyrotoxicosis, starting from the simple fixed dose regime to the highly complicated dosimetric evaluation prior to therapy. It may be noted that not all patients with Graves' disease will be cured with a single therapeutic dose of radioactive iodine. In a study by Chiovato et al, persistence of hyperthyroidism after radioactive iodine therapy was related to higher pretreatment levels of thyroid-stimulating antibodies (11). Higher dose of I-131 may be needed in a select group of patients; e.g., young patients with larger

thyroid glands, higher serum T-4 concentration, higher 24 hrs RAIU values and pre-therapy anti-thyroid drugs for greater than 4 months are at higher risk of treatment failure (12). The incidence of hypothyroidism from radioactive iodine (RAI) treatment is largely dependent on the dose of radioactive iodine, reaching around 20% or higher in the first couple of years post-treatment, and thereafter continuing at a rate of 3 to 5% per year (13).

Thyroidectomy is a definitive treatment for thyrotoxicosis. It should preferably be performed when the patient is euthyroid to decrease the perioperative cardiac risks. Surgery for Graves' disease is indicated in pregnant hyperthyroid patients intolerant to antithyroid drugs, breastfeeding patients, non-pregnant patients who refuse radioactive iodine therapy, children with Graves' disease, patients resistant to or allergic to radioactive iodine or antithyroid drugs, and patients with large or nodular goiter or with a cold nodule in active progressive ophthalmopathy (14). Total thyroidectomy is recommended increasingly to reduce the risk of recurrent hyperthyroidism (15). In terms of long-term cure rates, relief of hyperthyroidism is achieved in about 80% of children and adults after subtotal thyroidectomy. Hyperthyroidism recurs in about 10-15% of patients after subtotal thyroidectomy in comparison to an overall recurrence of less than 3 % in both children and adults after total thyroidectomy (16). Hypothyroidism develops in about 60% of individuals, who had subtotal thyroidectomy. However hypothyroidism is universal in those who had total thyroidectomy (16-17). Complication rates are comparable following subtotal or total thyroidectomy. The incidence of complications and the rates of recurrence of hyperthyroidism depend in large part on the skill and experience of the surgeon (17). Thyroid storm is a rare clinical emergency that is fatal when left untreated. Even with early diagnosis and aggressive treatment, mortality is still high at 20 to 30% (18, 19). The storm is usually due to a severe exacerbation of a preexisting thyrotoxicosis, which later leads to decompensation in different organ systems (20). In a previous case report, supraventricular tachycardia can be an unusual manifestation of thyroid storm (21). In our series, although all patients had large goiters, they did not have compressive symptoms. All three patients had radioactive iodine therapy, with the first two patients receiving single doses of < 10 mCi I-131, while the third patient had three doses of I-131 resulting in a cumulative dose of 23.5 mCi prior to surgery. The first two patients opted for surgery after a single dose RAI due to financial reasons. The surgery on the third patient was indicated because of persistent hyperthyroidism. All patients were biochemically euthyroid with normal free T4 levels prior to surgery. However, it appears that in the first two patients who received relatively low doses of I-131 (< 10 mCi) the free T-4 hormone levels were not the exact reflection of the euthyroid state. Hence medical complications like supraventricular tachycardia and thyroid storm ensued in

the perioperative period. On the other hand in the third patient who received the largest cumulated dose of I-131 (23.5 mCi) prior to thyroidectomy no perioperative complications were encountered.

Conclusion

This study is based on a very small group (only three patients) of patients and this may not be sufficient to draw any definitive conclusions. However, it appears that normalization of thyroid hormone values especially free T4 is not a sufficient guide for a good and uneventful outcome of thyroid surgery in severely hyperthyroid patients with large goiters. Radioactive iodine therapy may prove to be helpful in reducing or eliminating morbidity by inducing thyroid tissue fibrosis and true clinical euthyroidism, thereby resulting in excellent, event-free postoperative course. Further studies are needed to confirm our hypothesis, which is indeed based on a very small number of patients.

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