Iodine-131 Treatment of Graves' Disease Using Modified Early Iodine-131 Uptake Measurements in Therapy Dose Calculations

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We hypothesized that early uptake of iodine-131 (^{131}I) at 3–6 hr (EU) by the thyroid could be used to calculate ^{131}I therapy with results comparable to those obtained using late uptake of ^{131}I at 20–28 hr (LU) results. A retrospective study was undertaken. Twenty-seven patients with untreated thyrotoxic Graves' disease were given 3–5 μCi of ^{131}I and EU and LU were determined with an uptake probe. We derived a "best fit" curve on plots of EU (X-axis) and LU (Y-axis). The equation for the curve (LU = −55.7 + 73.2 log EU) was used to predict late uptake (PU) from EU results on a second group of 24 similarly defined Graves' patients. PU and measured LU were then applied to ^{131}I treatment calculations in these 24 patients. PU correlated closely with LU (r = 0.94). Dose calculations based on PU and LU gave very similar results (r = 0.97). Using this method, same day diagnosis and treatment of Graves' is achievable.

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Since its introduction in 1940, measurement of radioiodine uptake by the thyroid gland has been widely used in the assessment of thyroid function (*1–6*). The fact that normal values for thyroid radioiodine uptake changed as dietary iodine varied in the United States, resulted in a need for redefinition of the normal range during the 1970s (*7–8*). Evolution of precise indices of thyroid function, including sensitive measurements of thyroid stimulating hormone (sTSH), total and free thyroxine (T4) and triiodothyronine (T3) and detection of thyroid stimulating immunoglobulins (TSI) in the blood, have refined the process of thyroid diagnostic testing (*9–11*). At present, radioiodine uptake testing is less commonly relied upon to make a fine distinction between patients who are subtly hyperthyroid versus those who are euthyroid, than it is to make the distinction between patients whose hyperthyroxinemia is due to thyroiditis from those with Graves' disease or toxic nodular goiter (*12*). In thyroiditis, radioiodine uptake is characteristically nearly completely suppressed (*13*) whereas in thyrotoxicosis and toxic nodular goiter it is normal or high (*12,14*).

A further indication for radioiodine uptake measurements is to assist in calculation of treatment doses for patients with Graves' disease (*15,16*). Same day reporting of serum T_4, and sTSH is routinely available at our institution. The need for 24 hr measurements of iodine-131 (^{131}I) uptake by the thyroid—the traditional basis for calculation of ^{131}I therapy doses—still demands costly prolongation of hospital stay or return outpatient clinic visits in some patients. We hypothesized that the measurement of early uptake of ^{131}I by the thyroid could be used to calculate therapeutic doses of ^{131}I with results comparable to those obtained using the 24 hr ^{131}I uptake test results.

MATERIALS AND METHODS

Patients

The medical records of 51 patients (10 males and 41 females, mean age ± s.e.m. 46.9 ± 2.4 yr, range 16 yr to 84 yr were reviewed. All had diagnostic radioiodine uptake measurements at the Mayo Clinic Nuclear Medicine Laboratory between June 1988 and April 1989. Included in the study were only those who had both early (3–6 hr) and late (21–28 hr) uptake measurements. The clinical diagnosis of Graves' disease was supported in all instances by elevation of serum T_4 or T_3 with or without ancillary measurements of sTSH or TSI. Excluded were all patients who had previous radioiodine treatment, surgery or antithyroid drugs and those who were receiving T_4 or T_3 therapy. Patients who had received stable iodine solutions or radiographic contrast materials within the preceding 8 wk were also excluded, as were patients in whom the final diagnosis was subacute lymphocytic or subacute granulomatous thyroiditis, toxic solitary nodule or toxic multinodular goiter.

Since surgery and antithyroid drugs are very rarely used in the management of hyperthyroidism at the Mayo Clinic, we are not aware of any selection bias in the study group.

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All patients were evaluated by an experienced endocrinologist for clinical signs of Graves' disease, confirmation of the diagnosis, and for estimation of the weight (gm) of the thyroid gland.

T_4 and T_3 measurements were performed by radioimmunoassay. TSI measurements were performed with a cultured rat thyroid cell line (FRTL5) as described by Morris et al. (*10*). Sensitive TSH measurements were by chemiluminescence immunoassay (*11*).

An ^{131}I solution was prepared in the radiopharmacy for use as a tracer for routine diagnostic thyroid uptakes. The solution was calibrated to maintain a patient dose of 2–5 μCi (1 μCi = 3.7×10^4 Bq) in a volume of 0.3 to 0.5 ml. Following oral administration of 2–5 μCi ^{131}I solution, all patients were scheduled to return early (3–6 hr) and late (20–28 hr).

A Nuclear Chicago probe, with 3 × 3-in. crystal or an Atomic Products Corporation model 187 295 probe, with a 2 × 2-in. NaI crystal and a wide detector opening were used to measure ^{131}I uptake. All measurements were made with the crystal 25 cm distant from and centered on the thyroid cartilage or a standard. Room background was counted for 3 min followed by a 3-min count of an ^{131}I standard which was placed in a thyroid uptake phantom (Abbott-Orins Thyroid Uptake Phantom, No. 6782, Abbott Laboratories, North Chicago, IL). The standard was of the same volume and activity as the dose administered to the patient. The patient was then counted for 3 min and the thyroid uptake calculated according to the following equation:

$$\%\ \text{uptake of } {}^{131}I \text{ by the thyroid} = \frac{\text{neck counts} - \text{background}}{\text{standard counts} - \text{background}} \times 100.$$

Iodine-131 treatment dose calculations at the Mayo Clinic are based on the following formula:

$$\text{dose (mCi) to patient} = \frac{\text{gland size (g)} \times \text{dose requested } (\mu\text{Ci/g})}{\%\ \text{uptake of } {}^{131}I \text{ at 24 hr} \times 10}.$$

Note that the dose requested may be small (75 μCi/g), moderate (125 μCi/g) or large (200 μCi/g).

Statistics were performed on a MacIntosh 2 computer with Statview 512 and Cricket Graph software programs.

RESULTS

Twenty-seven of the 51 patients with Graves' disease were randomly selected to develop a method for defining the relationship between early and late uptake of ^{131}I. Early uptake of ^{131}I at 3–6 hr was plotted (X-axis) against late uptake of ^{131}I at 20–28 hr (Y-axis). The relationship between early and late uptake of ^{131}I was exponential. A "best fit" curve for early uptake (EU) versus late uptake (LU) of ^{131}I generated the equation:

$$LU = -55.7 + 73.2 \log EU \text{ (Fig. 1).}$$

Using the equation (LU = −55.7 + 73.2 log EU), late uptake of ^{131}I was predicted from early uptake of ^{131}I in the second group of 24 patients from the total study group of 51 patients with Graves' disease. Predicted late uptake of ^{131}I (PU) correlated closely (r = 0.94) with measured late uptake (LU) of ^{131}I (Fig. 2).

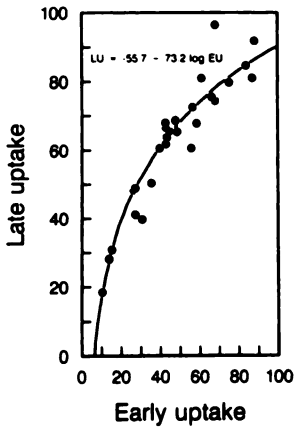

FIGURE 1
A plot of early uptake of ^{131}I (EU) on the X-axis and late uptake of ^{131}I (LU) on the Y-axis generated a best fit curve for the relationship between EU and LU. Equation for the curve: LU = −55.7 + 73.2 log EU.

PU was then used in dose calculations in the second group of 24 patients. Estimated doses based on PU were compared with therapy doses calculated from measured late uptake and actually administered to the patients. The predicted doses of ^{131}I correlated closely (r = 0.97) with given doses of ^{131}I (Fig. 3).

Mean treatment dose actually given and based on measured late uptake was 10.4 mCi and on predicted late uptake was 10.5 mCi. Application of unmodified measured early uptake results to the dose calculations resulted in an estimated mean dose which was 50% higher, with individual doses sometimes 100% greater than those derived from measured late uptake results.

DISCUSSION

Approaches to selecting radioiodine doses for the management of patients with Graves' disease vary widely. In some institutions, a fixed number of millicuries has been given to all patients (*17,18*) and in others an effort has been made to calculate delivered dose in terms of microcuries per gram of thyroid tissue (*19–21*). The number of microcuries per gram of tissue selected ranges from 50 to 200 or more. In addition to the wide variance in clinical perception as to how many microcuries of ^{131}I per gram of thyroid tissue constitute adequate treatment for thyrotoxic patients, dose calculation is further rendered inaccurate by the imprecision of the methods used to define how much thyroid tissue is actually present (*22*) and by the marked variation in radioiodine retention time in thyrotoxic glands (*23*). It is our impression that in light of the major imprecisions and inaccuracies in the other components of dose calculation, errors introduced by the use of early versus late thyroid radioiodine uptake results are relatively small. Accordingly, the test procedure for untreated Graves' patients could be modified to include only a single early uptake measurement without compromising patient care. We have not studied the reliability of

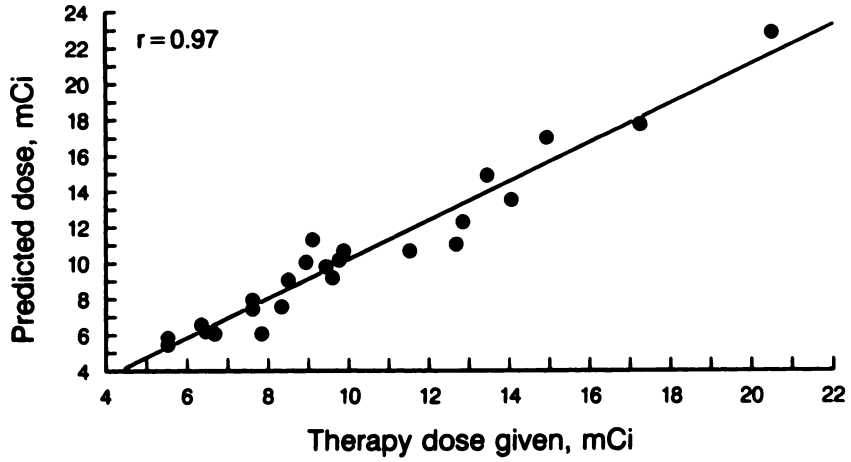

FIGURE 2
Using the equation LU = −55.7 + 73.2 log EU (Fig. 1), predicted values of late uptake of ^{131}I (PU) were obtained from early uptake measurements (EU). PU correlated closely with measured late uptake LU (r = 0.94).

our equation in patients who may have altered radioiodine kinetics due to therapy with antithyroid drugs, toxic multinodular goiter or who have undergone partial thyroidectomy.

A previous study has compared ^{123}I uptake measurement and scintigraphy at 4–5 hr with 24-hr uptake and scintigraphy in euthyroid, hyperthyroid, and hypothyroid patients. There was no overlap between euthyroid and hyperthyroid populations by the early uptake value. The authors concluded that for diagnostic purposes, the 4-hr uptake values were at least as useful as the 24-hr uptake values (*24*). Our study supports this observation.

The need for a 24-hr uptake value prior to radioiodine therapy in Graves' disease has previously been questioned. Four-hour values have already been used in therapy dose calculations with encouraging results. Only those patients whose 4-hr values were not clearly elevated, but who were clinically suspected of hyperthyroidism, were asked to return for a 24-hr value prior to therapy (*25*). In our view, differentiation between mild hyperthyroidism and euthyroid function can be made by measurement of T_4, T_3, sTSH and TSI rather than having to rely on the early and late ^{131}I uptake measurements to make this distinction.

We have shown in our study that the correlation between predicted late uptake (PU) and measured late uptake (LU) of ^{131}I is 0.94 and the correlation between doses based on PU and actual doses given based on LU is 0.97. For this reason we believe that in all patients with previously untreated Graves' disease, 24-hr ^{131}I uptake measurements to calculate therapeutic radioiodine doses are unnecessary.

Using the method described in this paper, same day measurement of ^{131}I uptake and radioiodine therapy is achievable with reduction in the cost of patient care and without compromise in its quality.

REFERENCES

1. Hamilton JG, Soley MH. Studies in iodine metabolism of the thyroid gland in situ by the use of radio-iodine in normal subjects and in patients with various types of goiter. *Am J Physiol* 1940; 131:135–143.
2. Raben MS, Astwood EB. The use of radioiodine in physiological and clinical studies on the thyroid gland. *J Clin Invest* 1949; 28:1347–1366.
3. Keating FR, Wang JC, Luellen TJ, Williams MM, Power MH, McConahey WM. The measurement of the iodine-accumulating function of the human thyroid gland. *J Clin Invest* 1949; 28:2:217–227.
4. Grayson RR. Factors which influence the radioactive iodine thyroidal uptake test. *Am J Med* 1960; 397–415.
5. Hamburger JI. Application of radioiodine uptake to the clinical evaluation of thyroid disease. *Semin Nucl Med* 1971;

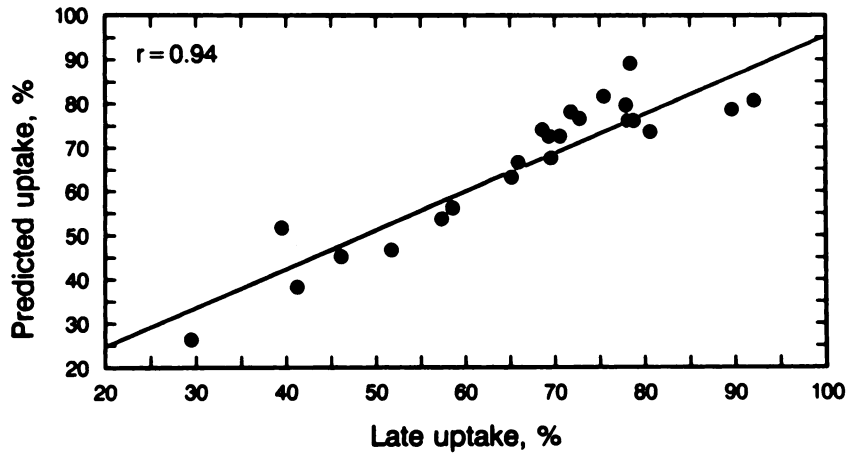

FIGURE 3
Predicted late uptake (PU) of ^{131}I (Fig. 2) was used in therapy dose calculations. Dose calculations using PU were compared with dose calculations using measured late uptake (LU) of ^{131}I and found to correlate closely (r = 0.97).

1:287–300.
6. Kaplan MM. Clinical and laboratory assessment of thyroid abnormalities. *Med Clin North Am* 1985; 69:863–880.
7. Caplan RH, Kujak R. Thyroid uptake of radioactive iodine. A reevaluation. *JAMA* 1971; 215:916–918.
8. Ghahremani GG, Hoffer PB, Oppenheim BE, Gottschalk A. New normal values for thyroid uptake of radioactive iodine. *JAMA* 1971; 217:337–339.
9. Evans M, Croxson MS, Wilson TM, Ibbertson HK. The screening of patients with suspected thyrotoxcosis using a sensitive TSH radioimmunoassay. *Clin Endocrinol* 1985; 22:445–451.
10. Morris JC, Hay ID, Nelson RE, Jiang N. Clinical utility of thyrotropin-receptor antibody assays: comparison of radioreceptor and bioassay methods. *Mayo Clin Proc* 1988; 63:707–717.
11. Bounaud MP, Bounaud JY, Bouin-Pineau MH, Orget L, Begon F. Chemiluminescence immunoassay of thyrotropin with acridinium-ester-labelled antibody evaluated and compared with two other immunoassays. *Clin Chem* 1987; 33:2096–2100.
12. Hay ID, Klee GG. Thyroid dysfunction. *Endocrinol and Metab Clin North Am* 1988; 17:473–509.
13. Teixeira VL, Romaldini JH, Rodrigues HF, Tanaka LM, Farah CS. Thyroid function during the spontaneous course of subacute thyroiditis. *J Nucl Med* 1985; 26:457–460.
14. Hamburger JI, Hamburger SW. Diagnosis and management of large toxic multinodular goiters. *J Nucl Med* 1985; 26:888–892.
15. Carpentier WR, Gilliland PF, Piziak VK, et al. Radioiodine uptake following iodine-131 therapy for Graves' disease: an early indicator of need for retreatment. *Clin Nucl Med* 1988; 14:15–18.
16. McFarland KF, Saleeby G. Graves' disease. Manifestations and therapeutic options. *Postgrad Med* 1988; 83:275–282.
17. Watson AB, Brownlie BE, Frampton JG, Turner JG, Roger TG. Outcome following standardized 185 MBq dose ^{131}I therapy for Graves' disease. *Clin Endocrinol* 1988; 28:487–496.
18. Ratcliffe GE, Fogelman I, Maisey MN. The evaluation of radioiodine therapy for thyroid patients using a fixed-dose regime. *Br J Radiol* 1986; 59:1105–1107.
19. Margouleff D. The radioiodine treatment of Graves' disease. Predictable unpredictability. *Clin Nucl Med* 1984; 1:50.
20. Orgiazzi J. Management of Graves' hyperthyroidism. *Endocrinol and Metab Clin North Am* 1987; 16:365–389.
21. Young RL, Nusynowitz ML. The treatment of benign thyroid disease. *Semin Nucl Med* 1979; 9:85–94.
22. Becker DV, Hurley JR. Current status of radioiodine (^{131}I) treatment of hyperthyroidism. In: Freeman LM, Weissman HS eds. *Nuclear medicine annual 1982*. New York: Raven Press. 1982:265–290.
23. Malone JF. Recent developments in dosimetry of radionuclides in the thyroid. In: Dumont JE, Malone JF, Van Herle AJ, eds. *Irradiation and thyroid disease (EU R-6713)*. Luxembourg: Commission of the European Communities; 1980.
24. Floyd JL, Rosen PR, Borchert RD, Jackson DE, Weiland FL. Thyroid uptake and imaging with iodine-123 at 4–5 hours: replacement of the 24-hour iodine-131 standard. *J Nucl Med* 1985; 26:884–887.
25. Cowan RJ, Ball JD, Watson NE. Efficacy of the four-hour radioiodine uptake determination prior to radioiodine therapy for hyperthyroidism [Letter]. *J Nucl Med* 1986; 2:309.