Iodine-131 Therapy of Hyperthyroidism in Pediatric Patients

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The purpose of this retrospective study was to evaluate the utility of $^{131}$I as therapy for hyperthyroidism in children and to evaluate its short-term side effects. Methods: The results of $^{131}$I therapy of hyperthyroidism were evaluated in a group of 35 pediatric patients. Results: In 29 patients propylthiouracil or methimazole therapy was abandoned due to noncompliance (13), relapse or failure to control hyperthyroidism (13), vasculitis (1), neutropenia (1) or a lupus-like syndrome (1). Average treatment activity was 7.7 ± 2.9 (s.d.) mCi, corresponding to 0.16 ± 0.03 mCi/kg. Thirty patients (86%) received a single radiiodine treatment and five (14%) were retreated. In patients who became hypothyroid after a single dose, hyperthyroidism was noted within 100 days of treatment. Clinical management problems included vomiting in four patients and enuresis in four patients. Mild radiation thyroiditis occurred in one patient and nodulopathy was noted after therapy in two patients. Conclusion: Iodine-131 is effective for both initial treatment of hyperthyroidism and the treatment of medical treatment failures in pediatric patients. Awareness of vomiting and enuresis as potential management problems is crucial when using $^{131}$I in this age group. Therefore, special treatment precautions may be required.

Key Words: radiiodine therapy; hyperthyroidism; iodine-131


Iodine-131 was first used for treatment of hyperthyroidism some 50 yr ago, but its use in pediatric patients has been far more limited than in the adult population. In adults, efficacy and short- and long-term side effects have been assessed in studies involving thousands of patients (1). In contrast, a relatively small number of pediatric patients have been evaluated in the literature to date (2–11). Many pediatricians have been hesitant to use $^{131}$I in children and have encouraged the use of medical therapy as the initial treatment of hyperthyroidism in this age group (12–20). The effectiveness of medical treatment for this condition has been limited. Remission rates have ranged from approximately 25% to 60% at 2 yr or more after treatment has started, and relapses frequently occur (17,19,20). Complications of medical therapy may also necessitate a change in treatment (21). Consequently, the use of $^{131}$I for the therapy of hyperthyroidism in pediatric patients continues to gain support (11,22,23). This study reviews our experience in the treatment with $^{131}$I of 35 pediatric patients with hyperthyroidism from 1986 to 1993. Emphasis was placed on the reasons for a change in medical treatment, efficacy of treatment, need for retreatment and development of hypothyroidism.

MATERIALS AND METHODS

The hospital records of 35 patients from the Children’s Hospital Medical Center in Cincinnati, Ohio, who received radioactive therapy for hyperthyroidism, were retrospectively reviewed. All patients carried the diagnosis of Graves’ disease, but two had evidence of coexistent Hashimoto’s thyroiditis. The patients included 25 females and 10 males, ranging in age from 6 to 19 yr. Thirty of the 35 were 10 yr of age or older at the time of initial $^{131}$I treatment. A diagnosis of hyperthyroidism was made by the referring physician prior to $^{131}$I treatment in all cases, based on clinical and laboratory criteria. All available $T_3$, $T_4$ and TSH serum values both preceding and following treatment with $^{131}$I were recorded, as were symptoms and signs reported at clinic visits. The type of initial treatment given and the reason for any change in treatment were noted. The following were recorded for the 35 patients with adequate records: the estimated thyroid gland mass (where available), 24 hr radiiodine uptake within the thyroid gland, dose of $^{131}$I given, dose per thyroid gland mass and the number of treatments. The time to development of either biochemical or clinical evidence of hypothyroidism and subsequent clinical course following treatment with $^{131}$I were examined. The follow-up time ranged from 2 to 61 mo, averaging 21 mo.

Thyroid status was evaluated according to the following factors:

1. Euthyroid patients were defined as those who had no clinical symptoms or signs of hypothyroidism or hyperthyroidism, and whose total $T_3$, $T_4$ and/or TSH values were within their normal ranges, which were 83 ng/dl–213 ng/dl, 5.6 µg/dl–11.7 µg/dl and 0.0–10.0 µIU/ml, respectively.

2. Hypothyroid patients either had at least one laboratory value which deviated appropriately from the normal range, or were noted to exhibit clinical signs or symptoms of hypothyroidism. Two patients did not show biochemical evidence of hypothyroidism before thyroid hormone replacement was initiated.
RESULTS

Thirty-five patients had complete or nearly complete medical records. Six patients received $^{131}$I as initial treatment; the other 29 for whom data were available received either propylthiouracil or methimazole initially. Medical treatment was abandoned in those 29 patients due to relapse or failure to control hyperthyroidism, noncompliance, vasculitis, neutropenia or a lupus-like syndrome (Table 1). The average 24 hr radiiodine uptake of all patients was 86% at the time of initial $^{131}$I treatment.

Initial oral treatment activities ranged from 5.0 mCi to 18.3 mCi, averaging $7.7 \pm 2.9$ (s.d.) mCi. The largest cumulative dosage given to a patient was 21.8 mCi. The average administered activity per gram of estimated thyroid gland mass in the 33 patients with recorded estimated thyroid weights was 0.161 $\pm 0.03$ mCi/g (Table 2).

Clinical management problems in the early post-treatment period included vomiting in four patients, which was severe in one patient. The vomiting appeared associated with recurrent hyperthyroidism in two patients, including the one with severe vomiting. Two patients, including the one with severe vomiting, vomited shortly after therapy. Measurements of retained $^{131}$I were made, and one patient received a supplemental treatment dose on the next day. Pre-existing enuresis required special precautions in four patients. One patient developed mild radiation thyroiditis. Follow-up for two patients was incomplete.

Twenty-nine (83%) received only a single radiiodine treatment for hyperthyroidism (Table 2). Five patients (14%), all of whom had received previous medical treatment, required one $^{131}$I retreatment for persistent hyperthyroidism an average of 9 mo after the initial $^{131}$I treatment. The need for treatment was anticipated in an 18-yr-old female who had received some medical treatment in the past and who presented with an estimated thyroid gland mass of 220 g at initial radiiodine treatment (−11 times normal).

Of the 33 patients with adequate follow-up data, all were successfully treated for hyperthyroidism. The sixth patient was transiently hypothyroid, but hyperthyroidism recurred; a second $^{131}$I treatment was given. Twenty-nine of the 33 patients (88%) developed hyperthyroidism. In patients who received a single treatment, hyperthyroidism occurred a mean of 3 mo after $^{131}$I treatment, with approximately 80% of the patients developing hyperthyroidism within 100 days of initial treatment (Fig. 1, Table 3). In one of these patients, hyperthyroidism occurred after $^{131}$I treatment when the patient was receiving propylthiouracil treatment. Four patients remained euthyroid 1.5, 2, 11 and 42 mo after $^{131}$I treatment. The rapid development of hy-

TABLE 1
Reasons for Abandonment of PTU or Methimazole Therapy

<table>
<thead>
<tr>
<th>Reason</th>
<th>No. of patients</th>
</tr>
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<tbody>
<tr>
<td>Noncompliance</td>
<td>13</td>
</tr>
<tr>
<td>Relapse or failure to control hyperthyroidism</td>
<td>13</td>
</tr>
<tr>
<td>Cutaneous vasculitis</td>
<td>1</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1</td>
</tr>
<tr>
<td>Lupus-like syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
</tr>
</tbody>
</table>

TABLE 2
Previously Reported and Current Results

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients (with follow-up)</th>
<th>Age range (yr)</th>
<th>Follow-up (yr)</th>
<th>Activity mCi</th>
<th>mCi/g</th>
<th>Euthyroid</th>
<th>Hypothyroid</th>
<th>Retreated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapman (2)</td>
<td>30 (30)</td>
<td>1–18</td>
<td>1–23</td>
<td>8/30 (27%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shelton (3)</td>
<td>18 (18)</td>
<td>1–20</td>
<td>6–15</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Starr (4)</td>
<td>73 (73)</td>
<td>2.5–18</td>
<td>10–18</td>
<td></td>
<td>31/73 (42%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kogut (5)</td>
<td>23 (16)</td>
<td>2–14</td>
<td>0.7–4.3</td>
<td>10/15 (67%)</td>
<td>5/15 (33%)</td>
<td></td>
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<tr>
<td>Chio (6)</td>
<td>32 (30)</td>
<td>7–15</td>
<td>3–15</td>
<td>2–39 mean 9.9</td>
<td>mean 0.095</td>
<td>14/30 (47%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hayek (7)</td>
<td>30 (30)</td>
<td>8–18</td>
<td>mean 9.2</td>
<td>22/30 (73%)</td>
<td>8/30 (27%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Goldsmith (8)</td>
<td>17 (17)</td>
<td>8–20</td>
<td>1–15</td>
<td></td>
<td>6/17 (35%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Safa (9)</td>
<td>87 (87)</td>
<td>5–24 mean 12.3</td>
<td>2.9–31 mean 9.8</td>
<td>0.100–0.200</td>
<td>35/76 (46%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Freitas (10)</td>
<td>51 (51)</td>
<td>6–18</td>
<td>mean 14.6</td>
<td></td>
<td>165/191 (86%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamburger (11)</td>
<td>191 (191)</td>
<td>3–18</td>
<td>10</td>
<td></td>
<td>14/51 (23%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current study (1995)</td>
<td>35 (33)</td>
<td>6–19</td>
<td>0–5</td>
<td>5.0–18.3 mean 7.7</td>
<td>mean 0.181</td>
<td>4/33 (12%)</td>
<td>29/33 (88%)</td>
<td>6/35 (17%)</td>
</tr>
</tbody>
</table>

FIGURE 1. For the 29 patients who developed hypothyroidism, the percent who had become hypothyroid is indicated for each time period following therapy.
on-thyroidism was unrelated to patient age, sex, or dose per gram of thyroid gland mass ($p = ns$).

Solitary nodules were noted in two patients 4 and 17 mo after $^{131}$I treatment. One was a 1–1.5 cm palpable nodule, with decreased uptake on $^{123}$I scintigraphy. Pathology demonstrated Hashimoto’s thyroiditis with a hyperplastic follicle. In the other patient, a 6–8 mm nodule, subsequently increasing in size to 1.0 cm, was palpated in the right neck 17 mo after original $^{131}$I treatment (24) just prior to retreatment. The nodule could not be seen on an $^{123}$I scan. Ultrasound of the thyroid confirmed the presence of this nodule and noted a small cyst within it. Subsequent fine needle biopsy was nondiagnostic; the patient did not return for a repeat biopsy.

**DISCUSSION**

The success of radiiodine in reversing hyperthyroidism demonstrated in this study is similar to that obtained in earlier studies. In the five studies where the administered activity per gram of thyroid tissue is known, 27%–92% of $^{131}$I treated patients became hypothyroid and 0%–40% required retreatment (Table 2). Eighty-three percent of our patients received only a single treatment with $^{131}$I. The reasons for abandonment of medical treatment encountered in this series (Table 1) reflect the limitations and side effects of medical management of hyperthyroidism (10,21,25).

The most notable early management problem after $^{131}$I in these patients was vomiting. The four patients with vomiting in this study included one who vomited within two hr of treatment. The retained radiiodine was measured and a second smaller dose was given on the next day. Because of a vasculitic reaction to propylthiouracil, propranolol was used to control the patient’s hyperthyroid symptoms. During protracted episodes of vomiting, the patient was unable to retain oral medication. Treatment with intravenous propranol, followed by use of a long-acting beta-blocker, resulted in improved control of the hyperthyroid symptoms during the post-therapy period and resulted in a cessation of the patient’s episodes of vomiting. Four patients had a history of enuresis; the radiation safety precautions taken included short hospitalizations for up to three days after treatment when there was uncertainty about the family’s ability to keep bedding and clothing free of radiiodine contamination.

The rapid development of hypothyroidism, observed in the majority of these patients, contrasts sharply with the time to onset of hypothyroidism in adults treated with $^{131}$I for hyperthyroidism. In the Cooperative Thyrotoxicosis Follow-up Study, 50% of patients who received 0.160 mCi per estimated gram of thyroid tissue were hypothyroid at 5 to 10 yr after therapy (25). The rapid appearance of hypothyroidism in our patients was found to be unrelated to dose per gram of thyroid gland mass, sex or age, and its cause remains unknown. It should be noted that avoiding the development of hypothyroidism following $^{131}$I therapy has been a major consideration for some (26–31), leading to pursuit of a dosage that would suppress hyperthyroidism without destroying the gland. Although lower doses have resulted in a lower incidence of hypothyroidism, retreatment has been required more frequently after these lower doses (Table 2). In recent years, some preference for higher doses has been noted (Table 2), along with correspondingly higher hypothyroidism rates.

Solitary thyroid nodules appeared shortly after therapy in two patients. In other series, small numbers of benign nodules have been noted after therapy, and many have demonstrated evidence of Hashimoto’s thyroiditis (Table 3).

**CONCLUSION**

The results of this present study support the use of $^{131}$I in treating hyperthyroidism in children and adolescents. Al-
though special treatment precautions may be required in this age group, the ease of administration, effectiveness and safety of $^{131}$I continue to make it attractive for initial treatment of hyperthyroidism.

REFERENCES


