Comparison of Outcomes After $^{123}$I Versus $^{131}$I Preablation Imaging Before Radioiodine Ablation in Differentiated Thyroid Carcinoma

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Detection of residual tissue after thyroidectomy for papillary or follicular thyroid carcinoma may be performed using diagnostic imaging with either $^{123}$I or $^{131}$I. The former is often preferred to avoid “stunning”—defined as a reduction in uptake of the therapeutic dose of $^{131}$I caused by some form of cell damage from the diagnostic dosage of the radionuclide. Stunning could potentially reduce the therapeutic efficacy of $^{131}$I given to ablate a postthyroidectomy remnant. This study examines the outcomes of ablative $^{131}$I therapy after diagnostic studies with either $^{123}$I or $^{131}$I to determine if the diagnostic dosages of these radionuclides used in our Thyroid Cancer Center reduce the efficacy of $^{131}$I given for remnant ablation. Methods: Fifty patients with nonmetastatic papillary or follicular carcinoma of the thyroid received total thyroidectomy; this was followed by thyroid hormone withdrawal to achieve a serum thyroid-stimulating hormone level in excess of 30 μIU/mL. They were divided prospectively into 2 groups. Group 1 had diagnostic imaging with 14.8 MBq of $^{123}$I followed by thyroid remnant ablation with 3.7 GBq of $^{131}$I. Group 2 had empiric ablation with the same 3.7-GBq $^{131}$I dosage, but the preceding diagnostic scan was performed with 74 MBq of $^{131}$I. Comparisons of equivalence of the 2 population samples and of the postablation outcomes were evaluated by $\chi^2$ analysis. Successful ablation required a negative follow-up thyroid scan 6–8 mo after ablation and also an undetectable serum thyroglobulin level in the absence of antithyroglobulin antibodies. Results: There was no significant difference between the 2 groups demographically, in tumor burden or stage, or in the postthyroidectomy ablation rate (group 1, 81%; group 2, 74%; $P > 0.05$). Conclusion: If thyroid remnant stunning occurs due to 74 MBq of $^{131}$I used as a diagnostic agent before $^{131}$I ablation, it has no significant clinical correlate, as it yields the same ablation rate as that which occurs after 14.8 MBq of $^{123}$I used for imaging.

Key Words: thyroid carcinoma; ablation; stunning; $^{123}$I-iodine; $^{131}$I-iodine

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RESULTS

Fifty patients were entered into the study, with one (from group 2) lost to follow-up. The patients of the 2 groups were found to be statistically comparable in age, sex, ratio of the number of papillary to follicular thyroid carcinomas, tumor burden, and locoregional metastases. None had distant metastases (Table 1). The mean activity of the ablative dosage of $^{131}$I was not significantly different between the 2 groups, averaging $3.77 \pm 0.11$ GBq.

These demographically similar groups had comparable scintigraphic rates of ablation (group 1, 88%; group 2, 91%; $P > 0.05$), but, using our second diagnostic criterion for complete ablation—that the quantitative measurement of serum tg had to be below detectable limits as well (unlike all but one of the studies to be discussed)—decreased our ablative success rate for group 1 to 81% and for group 2 to 74% ($P > 0.05$) (Table 2). Six patients in group 1 (23%) and 4 in group 2 (17%) ($P > 0.05$) had an elevated anti-tg antibody level, invalidating the serum tg test as a criterion of the completeness of ablation for these 10 patients.

DISCUSSION

We have demonstrated that if stunning from $^{131}$I occurred in our patients, as much of the relevant literature suggests, this phenomenon did not reduce the yield of complete ablation of thyroid remnants when compared with a statistically similar sample of patients we studied who received $^{123}$I as the diagnostic radionuclide. For the detection of residual normal tissue (not thyroid cancer), the $^{123}$I scan performed at 24 h is quite sensitive at the dosage we used.

We believe that a preablation radioiodine scan is important for several reasons: (a) about 2% of our patients have had a true total thyroidectomy by both scintigraphic evidence and the absence of measurable serum tg, and it is not justifiable to administer $\beta$-emitting radioiodine therapy to patients who do not need it; (b) staging with the preablation iodine dosage may reveal metastatic disease, a finding that then requires a higher therapeutic amount of iodine than originally planned; (c) some areas of iodine-concentrating metastatic disease may require special preparations—for example, corticosteroids before treating cerebral metastases.

Several problems became apparent on review of the relevant literature:

(i) The comparison groups were not always matched for age, sex, type of thyroid cancer, and diagnostic and therapeutic dosages of radioiodine;

(ii) If stunning was noted, it was usually confirmed only qualitatively, a process which can cause its own problems (4);

(iii) The great majority of papers in this field have judged the success of ablation solely from visual inspection of a follow-up scan 6 or more months after therapy with $^{131}$I; however, one must also require a negative assay for serum tg to exclude the presence of functioning thyroid tissue.

Stunning, as defined, was first demonstrated in 1951 (5), and this phenomenon has subsequently been reported in numerous papers and summarized in recent reviews (6,7). An inference from the observation of stunning is that the diagnostic dosage has interfered in some way with the trapping or retention of the therapeutic dosage or that the targeted mass has been reduced in volume and, hence, in uptake.

Numerous studies indicate that $^{123}$I is comparable to $^{131}$I in the detection of thyroid remnants after thyroidectomy (8–10). Park et al. studied patients after thyroidectomy with diagnostic dosages of 8.1 MBq of $^{123}$I or 111–370 MBq of $^{131}$I, with a subsequent ablative dosage of $^{131}$I ranging from 3.7 to 7.4 MBq (11). Using the 1-y follow-up scan, without a tg level, these workers reported that total ablation was

### TABLE 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1 ($^{123}$I, $n = 26$)</th>
<th>Group 2 ($^{131}$I, $n = 23$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillary/follicular carcinoma</td>
<td>22/4</td>
<td>21/2</td>
</tr>
<tr>
<td>Presence of anti-tg antibody (%)</td>
<td>6/26 (23%)</td>
<td>4/23 (17%)</td>
</tr>
<tr>
<td>Females/males</td>
<td>20/6</td>
<td>17/6</td>
</tr>
<tr>
<td>Mean age ± 1 SD (y)</td>
<td>$42.4 \pm 14.4$</td>
<td>$42.9 \pm 17.5$</td>
</tr>
<tr>
<td>Iodine uptake in neck remnant (%)</td>
<td>$3.7 \pm 2.8$</td>
<td>$4.1 \pm 3.1$</td>
</tr>
<tr>
<td>No. of patients with visualized neck node metastases on diagnostic scan</td>
<td>3/26</td>
<td>3/23</td>
</tr>
</tbody>
</table>

### TABLE 2

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group 1 ($^{123}$I)</th>
<th>Group 2 ($^{131}$I)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patient number</td>
<td>26</td>
<td>23</td>
</tr>
<tr>
<td>Complete ablation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scan only (%)</td>
<td>23 (88%)</td>
<td>21 (91%)</td>
</tr>
<tr>
<td>Scan + tg (%)</td>
<td>21 (81%)</td>
<td>17 (74%)</td>
</tr>
</tbody>
</table>
obtained in 75% of patients receiving 123I before the ablative dosage and 60% in those whose diagnostic tracer was 131I (P = 0.27). However, there is no indication what the mean ablative dosages were for these 2 groups and whether they were statistically different from each other. Park et al. did not observe stunning after they reduced the 131I activity administered to 74–111 MBq (11). 123I was used in the low dosages that Park et al. and our group administer provides excellent scintigraphic correlation with the 131I scintographs performed 7–10 d after ablation.

Several studies have found no evidence of stunning on ablation rate with 131I diagnostic activities of up to 185 MBq. The issue of stunning, and its clinical impact, may be related to the dosage of 131I used. Park et al. noted that qualitatively diagnosed stunning was not a problem at activities of 74–111 MBq (11).

Leger et al. imaged 51 patients after injection with 10–20 MBq (mean, 15.2 MBq) of 123I, 19 of whom also received 185 MBq of 131I on the same day, yielding 93% and 94% ablation rates, respectively, using only scintigraphic evidence (12). Although stunning was documented only qualitatively in the group receiving diagnostic 131I, there was no effect on the outcome (12). Dam et al. used an average therapeutic dosage of 131I of 4.58 ± 0.21 GBq after a diagnostic dosage of 185 MBq, with visual evaluation of decreased uptake (stunning) detected in 19% of patients 7 d after therapy (13). The follow-up ablation rate was 88% in patients whose scans showed no evidence of stunning and 91% (P > 0.05) in patients with stunning. However, 26% of patients were lost to follow-up, so information on the therapeutic outcome was available only in 74% (13). Karam et al. also found no difference in ablative outcome, whether a diagnostic dose of 92.5 or 185 MBq of 131I was used, with ablation in 78% and 74% of patients, respectively (P > 0.05), although the tg assay was not used (14). Similarly, Morris et al. noted no difference in the success rate of ablation after diagnostic 131I dosages between 111 and 185 MBq given before therapeutic activities of 3.7–7.4 GBq of 131I (65% ablated) as compared with a group that had no diagnostic scans and, thus, no exposure to potentially stunning 131I before treatment (67% ablated) (15).

In contrast to these 4 articles, 2 studies suggest a stunning effect of 131I, in activities of 111–185 MBq, on the outcome of ablation, but both have flaws that raise questions about the authors’ conclusions. Muratet et al. retrospectively reviewed 2 patient groups given diagnostic scanning dosages of either 37 or 111 MBq of 131I, which were then treated with 3.7 GBq of 131I (16). Follow-up studies performed 6.1–16.8 mo later revealed successful ablation in 50% of patients who had been scanned with 111 MBq of 131I and 76% success in the group receiving 37 MBq (P < 0.001). However, the group receiving the lower dosage was not matched for sex and contained a significantly higher percentage of men (16). In the second such study suggesting an effect of hypothesized stunning on outcome, Lees et al. retrospectively analyzed 3 patient groups that received, before remnant ablation with 3.7 GBq of 131I, a diagnostic scan dosage of 185 MBq of 131I, a diagnostic dosage of 740 MBq of 123I, or no diagnostic radioiodine. Visual evidence of complete ablation was present in only 47% of patients receiving 131I, 86% of those receiving 123I, and 83% of the group with no pretherapy exposure to a diagnostic dose of radioiodine. The 3 groups, however, had significant differences between them. The patients who received 131I for both diagnosis and therapy received a statistically larger amount of 131I therapy. The group with no pretherapy diagnostic scan had a mean serum tg of 10.7 ng/mL, whereas the first 2 groups had a far greater tumor burden with significantly higher tg values of 474 and 480 ng/mL, respectively. Follow-up after ablation imaging was performed as early as 3 mo after therapy when cell killing may not have been complete, so scintigraphy at this early time might lead falsely to the assumption of persistent (but mitotically sterile) tumor (17).

Finally, there is a study with the remarkable conclusion that the patients who experienced apparent thyroidal stunning had a better outcome than those who did not. Bajen et al. found that in 21% of patients studied, the posttherapy scan showed less uptake (stunning) qualitatively than on the diagnostic scans (18). A serum tg level of <3.0 ng/mL was used in this study, along with the radioiodine scan, to determine completeness of ablation. Sixty-two percent of stunned glands and only 37% of nonstunned glands were ablated according to these criteria. In this study, the therapeutic 131I dosage—ranging more widely than in any of the other studies (1.85–7.4 GBq) because patients with distant metastatic disease were included—was given an average of 7.2 wk after the diagnostic activity (185 MBq of 131I). This represents a far greater delay than in any of the other studies, wherein the time between diagnostic and therapeutic dosages of 131I was 1–9 d, except for that of Leger et al., which averaged 34 d with no evidence of an effect of stunning on ablation noted (12). Therefore, it is possible that enough time had passed for a therapeutic effect of the diagnostic activity to be added to the dosage actually given for treatment. The major problem in making any conclusions from the study of Bajen et al. arises from the fact that 23% and 26%, respectively, of the 2 groups had not yet had a follow-up scan (18).

There are also reports of diagnostic dosages of 123I with activities of 185–200 MBq causing the stunning phenomenon (19,20), presumably from Auger electrons emitted by 123I (21). However, despite the stunning phenomenon observed with both radiopharmaceuticals in a range of dosages, complete ablation of postthyroidectomy remnants can usually be successfully achieved.

We chose not to quantitate the uptake of therapeutic 131I given after diagnostic dosages of 123I or 131I because this has been reproducibly done so often previously. Many practices now use recombinant human TSH (rhTSH) routinely for thyroid remnant ablation, but this study began before local insurance companies made rhTSH available to
all patients. However, the lack of rhTSH usage should not have altered the results, because scintigraphy after thyroid hormone withdrawal or after rhTSH stimulation yields equivalent results (22).

Although $^{123}$I is frequently used to image patients with thyroid cancer before ablation, $^{131}$I remains an important diagnostic radionuclide if one must perform dosimetric studies to determine the largest safe dose that can be given or currently when rhTSH is used. Furthermore, $^{123}$I may not always be available in every area performing nuclear medicine, and thus we feel it is important to know an activity of $^{131}$I that may be given for diagnostic purposes without sequelae that could affect the therapeutic outcome.

**CONCLUSION**

This study has demonstrated that a preablative scanning dosage of 74 MBq of $^{131}$I yields the same thyroid remnant ablation rate as 14.8 MBq of $^{123}$I, confirmed not only by the follow-up scan at 6–8 mo but also by a simultaneous undetectable level of serum tg. This is the first prospective study, to the author’s knowledge, of the clinical import of radioiodine-induced stunning with the $^{123}$I and $^{131}$I groups matched for age, sex ratio, tumor type and stage, and ablation dosage, and with virtually complete (98%) patient follow-up. If one must use $^{131}$I for preablative scanning, 74 MBq appears to be an appropriate activity that does not lower the ablation rate as compared with $^{123}$I.

**REFERENCES**


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