Thyroid Stunning After Diagnostic Dose of 185 MBq (5 mCi) Iodine-131 in Patients with Differentiated Thyroidal Cancer

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ABSTRACT

Thyroid stunning has been reported as a temporary impairment of thyroid tissue after diagnostic radioiodine (131I) dose that decreases the final absorbed dose in ablative 131I therapy. The aim of this study was to determine whether a 185 MBq (5 mCi) diagnostic dose of 131I produces a stunning effect on thyroid remnant before 131I ablative therapy in patients with differentiated thyroid cancer.

Patients and methods: Forty-eight patients with differentiated thyroid cancer following total or near-total thyroidectomy with no evidence of distant metastases were included in this study. Our patients were classified into 3 groups according to the time of ablation therapy. The 3 groups were patient group 1 (PG1), patient group 2 (PG2) and patient group 3 (PG3) when ablation therapy was administered at 3, 7 and 14 days after diagnostic dose of 5 mCi 131I, respectively. An ablative dose of 30-100 mCi 131I was administered 3-14 days after diagnostic dose. Uptake over thyroid remnant was assessed 72 hours post-diagnostic and post-ablation using single head gamma camera.

Results: In PG1, the mean post-diagnostic and post-ablative uptake values were 8.87% and 7.93% respectively with no significant difference (p > 0.05). However, in PG2 the post-ablation uptake was equal to 4.82% and was significantly lower (p < 0.001) than the previous diagnostic measurement (9.1%). Also, uptake of the ablative dose (4.21%) was significantly lower (p < 0.001) than the diagnostic uptake (8.23%) in PG3. The therapy/diagnostic uptake ratios in PG2 and PG3 (53% and 51% respectively) were significantly lower (p < 0.001) than that in the first group (89%). There was a good correlation between the visually apparent and quantitatively measured uptake when comparing post-ablation and post-diagnostic 131I studies.

Conclusion: Our data suggested that qualitative and quantitative assessment of gamma camera studies showed no evidence of stunning when the ablative dose was given within 72 hours from the diagnostic study of 185 MBq (5 mCi) 131I. However, stunning was evident with a delay of more than 3 days between the ablative and diagnostic activities of radioiodine.

Key Words: Thyroid stunning - 131I-Differentiated thyroid cancer.

INTRODUCTION

Iodine-131 (131I) plays an important role in the management of patients with well-differentiated thyroid cancers. Post-thyroidectomy ablation therapy with 131I is performed to destroy the small amount of thyroid tissue remaining in the neck after surgery [8,14]. The use of radioiodine for ablation has been shown to decrease the risk of recurrence, increase the sensitivity of post-ablation whole-body scanning with radioiodine and increase the sensitivity of serum thyroglobulin testing [12]. In patients being considered for ablation therapy, a pre-treatment diagnostic 131I scan is performed 5 to 6 weeks following surgery to assess the presence of metastatic lesions. Iodine-131 given for a diagnostic scan can exert a negative effect on the uptake of the therapeutic dose by residual thyroid bed tissue and functioning metastases. This is referred to as (thyroid stunning). The (Stunned) thyroid tissue then loses its iodine trapping function partially or completely. This is a radiobiologic phenomenon and the degree of stunning depends on the absorbed radiation dose. In fact, the higher the diagnostic dose used, the greater the possible subsequent decrease in uptake of the therapeutic dose [25]. While some findings support the concept of stunning, other authors have found no evidence of stunning for diagnostic 131I activities in the range of 37-370 MBq [11,13,15,21,22,26]. Due to inherent difficulties in the exact volumetric determination of remnant or metastatic tissue, it is very difficult to quantify just how much of the diagnostically administered radioiodine is actually absorbed.
by this tissue. For this reason, all efforts have centered around correlating the extent of potential stunning with the magnitude of the diagnostic \(^{131}\text{I}\) activity administered \(^{23,24}\).

The purpose of this study was to determine whether 185 MBq (5 mCi) \(^{131}\text{I}\) may be capable of producing a stunning effect on thyroid tissue that may interfere with the uptake of the subsequent ablative dose of radioiodine.

**PATIENTS AND METHODS**

Forty-eight patients with differentiated thyroid cancer (18 males, 30 females with mean age of 43±10 years) following total or near-total thyroidectomy were studied. There was no evidence of distant metastases as proved by chest radiography, abdominal ultrasonography. Computed tomography and bone scan were used for 19 patients to exclude metastatic lesions. Six weeks after surgery, all patients received 185 MBq (5 mCi) \(^{131}\text{I}\) for diagnostic purposes followed by a whole body scan at 72 hours. They were randomly divided into three groups according to \(^{131}\text{I}\) ablation time. Patient group 1 (PG1) composed of 16 patients who received ablative dose of radioiodine at the same day of diagnostic scan (72 hour after oral intake of diagnostic activity). Patient group 2 (PG2) included 16 patients with ablative dose administered one week after the diagnostic dose. Patient group 3 (PG3) had 16 patients who received ablative radioiodine dose two weeks after diagnostic dose. Ablative dose ranged from 1110-3700 MBq (30-100 mCi) according to the volume of residual thyroid tissue remaining. Qualitative and quantitative assessments of uptake were considered for all patients at 72 hours of ablative dose of \(^{131}\text{I}\).

**Scanning techniques and data acquisition:**

All patients were scanned using a single head gamma camera with a high energy parallel-hole collimator. Total body scans were performed 72 hours after diagnostic and ablative doses at a scan speed of 10 cm/min. Both anterior and posterior projections were obtained. Spot views (anterior neck) were also obtained for 15 min/view. Post-ablation scan was compared with the previous diagnostic scan for any visual evidence of stunning. After acquisition, uptake in the thyroid bed was assessed following diagnostic and ablative scans. Appropriate thyroid and background regions of interest were drown to allow measurement of uptake for diagnostic study. These regions were stored and employed for the post-ablation study. The diagnostic uptake was compared with the early (72 Hr.) and late (7-14 days) ablative uptake values then ablation/diagnostic uptake ratio was assessed in each group.

**RESULTS**

This study included 48 patients with differentiated thyroid cancer presented to nuclear medicine department after total or near-total thyroidec tomy for further management. Papillary carcinoma was detected in 33 patients (69%) (12 male and 21 female) and follicular carcinoma was reported in 15 patients (31%) (6 male and 9 female). The mean age at the time of diagnosis was 38±9 years for papillary and 49±7 years for follicular carcinoma (Table 1). Thirty-one patients (65%) with small remnants of thyroid tissue (10 in PG1, 9 in PG2 and 12 in PG3) received low dose regimen of 30 mCi \(^{131}\text{I}\). On the other hand 17 patients (35%) with a big thyroid tissue remnants (6 in PG1, 7 in PG2 and 4 in PG3), received a high dose regimen of \(^{131}\text{I}\).

The discrepancy of radioiodine uptake between imaging studies after diagnostic and ablative doses of radioiodine was assessed visually and the degree of stunning was quantified by comparing the initial percent of uptake using the diagnostic dose and a second uptake obtained after ablative doses of radioiodine. Visually, there was no detectable reduction in the radioiodine uptake after ablative doses as compared with that after diagnostic doses in PG1 (Fig. 1). However, apparently reduced uptake in thyroid remnants was observed in all 32 patients in PG2 and PG3 (Fig. 2). Quantitative evaluation of the degree of uptake showed that there was reduced uptake of the ablative radioiodine in all 48 patients included in this study. Also, there was a good correlation between the visual and the quantitative evaluation of all patients (Table 2). Visual interpretation showed that there were two false negative images due to complete stunning in PG3 (Fig. 3).

In PG1, quantitative studies showed that, there was no significant difference between the mean diagnostic (8.87%) and ablative (7.93%) uptake values of radioiodine (p > 0.05). However, in PG2, the mean uptake of ablative doses of \(^{131}\text{I}\) was (4.82%) and it was significantly lower than the previous diagnostic uptake of radioio-
The ablative/diagnostic uptake ratios for the 3 groups were 89%, 53% and 51% respectively with significant difference when comparing the ratio in PG1 with that in PG2 or PG3 (Table 3). On the other hand, there was no statistical difference between the radioiodine uptake after diagnostic doses in the 3 groups (8.87% in PG1, 9.1% in PG2 and 8.23% in PG3) (p > 0.05). Moreover, there was no significant difference in the uptake values after ablative regimens of radioiodine between patients in group 2 (4.82%) and patients in group 3 (4.21%) (p > 0.05).

The mean uptake value in thyroid bed after the early (within 72 hours after diagnostic activity) ablative doses of radioiodine was 8.33% for papillary carcinoma and 7.7% for follicular carcinoma with no statistical difference (p > 0.05). Also, after delayed ablative doses of radioiodine, the uptake in thyroid remnants for papillary carcinoma was 4.27% and 4.97% in PG2 and PG3 respectively. For follicular carcinoma, the radioiodine uptake after ablative doses was 5.39% and 4.01% in PG2 and PG3 respectively. There was no significant difference in the mean uptake values between papillary and follicular carcinomas in PG2 and PG3 (p > 0.05) (Table 4). The mean uptake after low dose of ablative radioiodine (30 mCi) for PG1, PG2 and PG3 were 8.22%, 4.39% and 4.18% respectively. Whereas, the mean radioiodine uptake for high dose regimen (100 mCi) was 7.82%, 5.44% and 4.27% for PG1, PG2, PG3 respectively. In each of the three patient groups, there was no significant difference in the radioiodine uptake between low and high dose regimens (p > 0.05) (Table 5).

Table (1): Age and sex distribution of differentiated thyroid cancer.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Papillary type</th>
<th>Follicular type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Female</td>
<td>21</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>15</td>
</tr>
<tr>
<td>Mean age</td>
<td>38±9 years</td>
<td>49±7 years</td>
</tr>
</tbody>
</table>

Table (2): Correlation between visual and quantitative assessment of thyroid stunning.

<table>
<thead>
<tr>
<th>Stunning</th>
<th>Visual assessment</th>
<th>Quantitative assessment</th>
<th>Interval between 1st and 2nd uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>16</td>
<td>16</td>
<td>3 days</td>
</tr>
<tr>
<td>Incomplete</td>
<td>30</td>
<td>30</td>
<td>7-14 days</td>
</tr>
<tr>
<td>Complete</td>
<td>2</td>
<td>2</td>
<td>14 days</td>
</tr>
</tbody>
</table>

Table (3): The mean uptake values uptake after diagnostic and ablative doses of radioiodine with ablative/diagnostic uptake ratios.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Uptake</th>
<th>p value</th>
<th>Ablative/diagnostic uptake ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diagnostic</td>
<td>Ablative</td>
<td></td>
</tr>
<tr>
<td>PG1</td>
<td>8.87%</td>
<td>7.93%</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>PG2</td>
<td>9.1%</td>
<td>4.82%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PG3</td>
<td>8.23%</td>
<td>4.21%</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Table (4): Uptake in thyroid remnant in relation to the histopathologic types of differentiated thyroid cancer.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Papillary</th>
<th>Follicular</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PG1</td>
<td>8.33%</td>
<td>7.7%</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>PG2</td>
<td>4.27%</td>
<td>5.39%</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>PG3</td>
<td>4.97%</td>
<td>4.01%</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

Table (5): Uptake in thyroid remnant in relation to dose of ablative radioiodine.

<table>
<thead>
<tr>
<th>Patients</th>
<th>30 mCi</th>
<th>100 mCi</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PG1</td>
<td>8.22%</td>
<td>7.82%</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>PG2</td>
<td>4.39%</td>
<td>5.44%</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>PG3</td>
<td>4.18%</td>
<td>4.27%</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>
Fig. (1): Thyroid scintigraphies post diagnostic dose (A) and post ablative dose (B) of radioiodine showed no apparent reduced uptake in thyroid remnant after ablative therapy.

Fig. (2): Thyroid scintigraphies post diagnostic dose (A) and post ablative dose (B) of radioiodine showed partial stunning, in post ablative scan.

Fig. (3): Thyroid scintigraphies post diagnostic (A) and post-ablative dose (B) of radioiodine showed complete stunning in the post ablative scan.
DISCUSSION

Iodine-131 is the most specific radionuclide to follow-up patients with differentiated thyroid cancer (DTC) [16]. The radioablation of thyroid remnants improves the prognosis of differentiated thyroid cancer [7]. Several authors have suggested that a scanning dose of 185-370 MBq (5-10 mCi) 131I may be capable of producing a stunning effect on thyroid tissue that may interfere with the uptake and efficacy of the subsequent ablation dose of radioiodine [5,21,29]. Such a reduction can result from (a) a decrease in the iodine uptake potential of thyroid cells, as well as a change in iodine turnover [24] or (b) a reduction in functional thyroid cells after 131I imaging, as some cells may have been damaged by beta emission of radioiodine [15]. There is an indication that the degree of stunning, resulting from the diagnostic administration of 131I, may intensify with time up to 25 days and then diminish as the thyroid remnant begins to recover from the effect of the diagnostic 131I. This data suggest that stunning is a transient effect and in due time, the thyroid remnant may regain its ability to trap and retain radioiodine [19].

Sixty-five percent of our patients received 30 mCi 131I for ablation of small thyroid remnants whereas, 35% of patients received high ablative dose of radioiodine (100 mCi) after total or near-total thyroidectomy. The activity of radioiodine used for ablation of thyroid remnants is not standardized and several treatment options exist [2]. For small remnants of thyroid, 30 mCi is as adequate as larger doses. Patients do not require hospitalization and up to 27% of patients will have successful ablation after only one dose of 30 mCi [6]. Out of the 48 patients in our study, 32 (67%) had scintigraphic pattern of apparently decrease uptake in thyroid remnants by visual evaluation. Other study of Kao and Yen [13] showed that 73.5% of patients had visually apparent decreased uptake in thyroid bed after therapeutic dose of 131I whole body scan.

In our study, the quantitative assessment showed that in PG1, there was no significant difference in uptake between post-ablative (7.93%) and pre-ablative (8.87%) doses with ablative/diagnostic uptake ratio of 89%. This finding suggested that there was no evidence of stunning when ablation with radioiodine performed within 72 hours of diagnostic activity. On the other hand, in PG2 and PG3, the post-ablation uptake was significantly lower than the diagnostic uptake when patients received radioiodine therapy 1-2 weeks after diagnostic activity denoting stunning effect. Several researches demonstrated evidence of stunning in post-therapy 131I scans with less uptake value than diagnostic scan if ablative dose was not administered in the same day of 5 mCi diagnostic 131I scan [11,15,23,30]. Also, other quantitative reports proved decreased therapeutic versus diagnostic efficacy per administered 131I unit [1,10,11,18,27,31]. Furthermore, Yaakob et al. [29] reported that diagnostic doses of 131I larger than 3 mCi will cause some cell injury to the tissue in which it decreases its 131I concentration and reduce subsequent uptake of 131I administered therapeutically. According to Leger et al. [15], stunning could result from a reduction of functional thyroid cells after 131I imaging, as some cells may have been damaged by beta emission of radioiodine. Because of the potential suppressive effect of the radiation from a diagnostic administration of 131I on the uptake of a subsequent therapeutic administration, many centers limit the amount given for scanning to 2-3 mCi [3,12,28].

While some findings support the concept of stunning, other authors have found no evidence of stunning after diagnostic 131I activities in the range of 37-370 MBq (1-10 mCi) [1,9,13,17,22,32]. Other data of Cholewinski et al. [4], Hilditch et al. [10] and Medvedec [19] showed that diagnostic whole body scanning can be performed effectively with a 185-MBq (5 mCi) dose of 131I if administered 72 hours before radioiodine ablation without concern for thyroid stunning.

In our study, all 32 patients who received ablative radioiodine at 1-2 weeks after diagnostic dose had significant stunning with reduction of the post-ablative uptake to 51%-53% of the diagnostic uptake. Also, Hilditch et al. [10] showed that reduced uptake of the ablative radioiodine was observed in all patients. The mean reduction was 32.8%. However, Kao and Yen [13] showed that the stunning effect was observed in 73.5% of patients who received diagnostic radioiodine dose of 185 MBq. Also, Yeung et al. [31] used gamma camera to measure uptake of the diagnostic and ablation activities of 131I in patients with differentiated thyroid cancer and reported that 81% of patients exhibited reduced uptake. The mean reduction
was 50% for the diagnostic activities. However, Medvedec [19] showed that the mean reduction in therapeutic uptake was 24% and 68% for average diagnostic absorbed doses of 10 to 40 Gy, respectively.

Another approach to avoid the problem of stunning associated with 131I is to prolong the time interval between diagnostic and therapeutic doses for several days to as much as 6 weeks [13,21,24]. Also, Leger et al. [15] showed decrease in thyroid uptake for several weeks after 131I administration and recommended postponing therapy in thyroid cancer patients for at least 5 weeks. In the patients given diagnostic 131I, stunning appeared to increase in severity as the time interval between the diagnostic and therapeutic radionuclides has pronged, for intervals up to 25 days. Thereafter, there seemed to be some recovery of uptake capability. These data suggest that stunning is a transient effect and in due time the thyroid remnant loses its ability to trap and retain radiiodine [10,19]. This is in keeping with the impression of Modoni et al. [20] that the degree of stunning is a function of the time delay between the two administrations of 131I and may be less for time intervals of > 20 days.

In conclusion, diagnostic whole body scanning can be performed effectively with 185 MBq (5 mCi) dose of 131I if administered 72 hours before radioiodine ablation without concern for thyroid stunning. Also, the degree of stunning is a function of time delay between the two administrations of 131I and may be significantly evident for time interval of more than 3 days from the diagnostic activity. This conclusion was based on a qualitative and quantitative assessment of the diagnostic and post-ablation images.

REFERENCES


