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Outcome of ablation of thyroid remnants with 100 mCi (3.7 GBq) iodine-131 in patients with thyroid cancer

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A retrospective study was conducted on 186 patients with differentiated thyroid cancer without metastases who received an ablative dose of 100 mCi (3.7 GBq) iodine-131 after total thyroidectomy. Six months to one year after ablation, 155/186 patients (83%) had a negative scan. Diagnostic scanning with 5 mCi (185 MBq) performed 72 h or 3 months before ablation did not interfere with treatment success compared to patients not submitted to pre-therapy scanning. Pre-ablation cervical uptake values < 2% were associated with a higher ablation efficacy (94%), from 2 to 5% showed 80% success and values > 5%, 60% ($p < 0.05$). There were no significant differences between the responsive and no responsive groups in terms of age, sex, histological type or size of the primary tumor. 11% of the patients with low stimulated Tg (< 2 ng/m*l*) presented discrete thyroid bed uptake on follow-up diagnostic scan (< 0.5%) without definitive residual disease and 89% had negative uptake on scan. The patients with Tg > 2 ng/m*l* presented thyroid bed (10/12) or ectopic (2/12) uptake on follow-up diagnostic scan. An ablative dose of 100 mCi shows a high rate of efficacy, especially when cervical uptake is < 2%; no difference was noted between patients assessed by scan within 72 h or 3 months before treatment and those not scanned; follow-up diagnostic scan can be avoided in low risk patients with stimulated Tg < 2 ng/m*l*.

Key words: ablation, thyroid remnants

INTRODUCTION

Initial treatment of differentiated thyroid carcinoma (DTC) consists of total thyroidectomy followed in most cases by ablation of normal and/or tumor remnants with iodine-131.[1–3] However, the dose necessary for ablation of cervical remnants is still a matter of controversy, ranging from 30 mCi (1.1 GBq) to 100 mCi (3.7 GBq). The application of low doses, most commonly 30 mCi, has some advantages: it does not require hospitalization, is of low cost, induces fewer adverse effects caused by radioactive iodine, and results in a satisfactory outcome when the remnants are discrete.[4–10] However, low doses are less efficient than high doses in cases of patients with significant remnants.[9,11] The dose with the best cost-benefit ratio remains undefined, despite the tendency towards the use of high doses.[9,12,13] Important factors that influence the efficacy of radioiodine treatment include the remnant mass which is inversely correlated with the success of ablation[4,5,8,9] and the stunning effect.[14–19] Due to the lower sensitivity of the 2 mCi (74 MBq) dose,[20] although it does not cause stunning,[21] we adopted a 5 mCi (185 MBq) tracer dose for diagnostic scanning, and therapy was usually initiated within 72 h[22,23] or after 3 months.

The objective of the present study was to determine the efficacy of a 100 mCi dose for ablation of thyroid remnants; the influence of pre-therapy scanning; correlation between cervical uptake and efficacy; and the necessity of diagnostic scan for the patients with low serum Tg in the follow-up after remnant ablation.

MATERIALS AND METHODS

We retrospectively analyzed 186 patients (136 women

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and 50 men; ranging in age from 13 to 78 years, 41.2 ± 14.7 years), with differentiated thyroid carcinoma (123 papillary carcinoma, 52 follicular carcinoma and 11 Hürthle cell carcinoma) seen at the Santa Casa de Belo Horizonte, Brazil, between 2000 and 2003. All patients underwent total thyroidectomy and only the first ablative treatment was considered for analysis. The selected patients included those with tumor size > 1.5 cm,[3] without lymph nodes or distant metastases (surgical stage, scanning, radiography, ultrasound, computed tomography) and who received 100 mCi (3.7 GBq) iodine-131 three to eight months after surgery (mean 6 months). When a diagnostic scan was performed, treatment was initiated within 72 h or after at least 3 months. Successful ablation was defined as no uptake on control follow-up diagnostic scan, 6 months to one year after ablation.

The study was approved by the Research Ethics Committee of our institution.

Thyroglobulin measurement

Thyroglobulin (Tg) was measured by a radioimmunometric assay (ELSA-hTg, CIS Bio International, France) with a functional sensitivity of 0.9 ng/m*l*, intra-assay precision of 2.4–6.6% and interassay precision of 5.1–8%, with the reference value established by the manufacturer being 3 to 42 ng/m*l*. All patients showed TSH levels > 30 mIU/*l* after withdrawal of T4 for 5 weeks. Antibodies (TgAb) were determined by a chemiluminescent assay (Chemiluminescent ICMA, Nichols Institute Diagnostics, San Juan Capistrano, CA) with a detection limit of 1 IU/m*l* and intra- and interassay precision of 8.7 and 5.9%, respectively, for values of 2 to 40 IU/m*l*.

Imaging methods

Diagnostic scanning was performed with a tracer dose of 5 mCi (185 MBq) iodine-131 during hypothyroidism after T4 withdrawal for 5 weeks and administration of a low iodine diet during the 2 weeks preceding the exam. Images of the whole body were obtained 72 h after iodine administration. Post-therapy scanning was performed 7 days after administration of the ablative dose as described above. All patients were scanned using a gamma dual head camera device (Varican GE) with 364-keV rated collimators. The sensitivities (counts per unit time) of both heads were also similar and adequate with National Electrical Manufacturers Association (NEMA) specifications. Total body scans were performed at a scan speed of 10 cm/min, step and shoot mode with body contour option. Both anterior and posterior views were obtained and spot views were also obtained for 15 min/view. Uptake in the thyroid bed was measured using a dual-head gamma camera. Scans were analyzed by three experienced professionals in nuclear medicine. Other imaging methods used for the definition of disease status were cervical ultrasound, contrast-free chest and mediastinum computed tomography and radiography, bone radiography and MIBI-scan.

Statistical methods

Significance was determined by χ^2 analysis and values $p < 0.05$ were considered significant.

RESULTS

178/186 patients (95.7%) showed thyroid bed uptake on post-therapy scan, and no ectopic uptake was visualized. Successful ablation (no uptake on follow-up diagnostic scan) was achieved in 155 patients (83%). The efficacy of ablation in patients subjected to pre-therapy scanning was 78.5% (33/42 patients) in those subjected to treatment within 72 h and 82% (41/50 patients) in those treated after 3 months. These results did not differ significantly from those obtained for 94 patients not subjected to diagnostic scanning (86%, p ns). Postoperative cervical uptake was determined before ablation in 90 cases. Cervical uptake < 2% (mean of 1.55%) was associated with 94% efficacy (47/50), uptake between 2 and 5% (mean of 3.4%) with 80% success (16/25), and uptake > 5% (mean of 7.11%) with 60% efficacy (9/15), $p < 0.05$. There were no statistically significant differences between the responsive and no responsive groups in terms of age, sex, histological type or size of the primary tumor. Serum thyroglobulin levels during hypothyroidism in the absence of anti-Tg antibodies were available for 120 patients in the follow-up after ablation. Of these, 80% (96 patients) had a negative uptake on follow-up diagnostic scan. However, when a thyroglobulin < 2 ng/m*l* was established as a criterion, the efficacy was 90% (108/120 patients). 12/108 patients (11%) with low Tg presented discrete thyroid bed uptake on scans (< 0.5%) without definitive residual disease. 12 patients with Tg > 2 ng/m*l* presented thyroid bed (n = 10) or ectopic (n = 2) uptake on follow-up diagnostic scan.

DISCUSSION

Postoperative iodine-131 therapy should be used selectively. In low-risk patients, the long-term prognosis after surgery alone is so favorable that iodine-131 ablation is not usually recommended.[3] However, all patients who are at high risk for recurrent disease should be treated with iodine-131, because it decreases both recurrence and death rates. We recommend iodine-131 therapy to all patients with tumor size > 1.5 cm,[2] extra-thyroid invasion, lymph node or distant metastases.

Comparative studies have shown that the efficacy of ablative therapy seems to be lower when a 30 mCi dose is used compared to high iodine-131 doses.[9,11] However, the lower dose might be effective in cases in which only discrete remnants are present.[4–10] A meta-analysis revealed that the difference between low and high doses is smaller in patients subjected to total thyroidectomy.[9] The 100 mCi dose demonstrated efficacy in agreement with other studies,[9,12,13] but doses higher than 30 mCi and lower than 100 mCi might be equally effective.[7,8,11,24,25]

A plateau of efficacy seems to be established at 50 mCi[24] and a dose of 60 mCi is associated with high ablation rates.[11] Doses higher than 100 mCi are not necessary for the ablation of thyroid remnants only[12] and fractionated doses of 30 mCi represent an alternative for ambulatory treatment.[26,27] We adopt a dose of 100 mCi for most cases without metastases, but we recognize that no convincing evidence exists to definitively abandon lower doses.[5]

An inverse relationship between cervical uptake and the success of radioiodine therapy was observed, as also demonstrated in other studies with high[5,28] and low doses.[4,5,11] However, cervical uptake as a predictor of the success of ablation has not been confirmed in other studies, especially those employing high doses,[11,29–31] probably due to the efficacy even in cases of higher uptake. Based on the present results, cervical uptake less than 2% seems to be ideal considering the high success rate obtained with 100 mCi (94%). Considering this amount of residual tissue, Cailleux et al.[13] obtained a success rate of 92% in 256 patients who received 100 mCi. We emphasize that low uptake is easily obtained after almost total thyroidectomy when performed by experienced surgeons.[32–35]

The impact of the stunning effect on ablation was assessed by determining the treatment efficacy in patients subjected or not to pre-therapy scanning. The occurrence of the stunning effect is known to be influenced by factors such as the dose used for diagnostic scanning, the interval between this exam and treatment, the therapeutic dose prescribed, and the definition of stunning itself which can be based only on a reduction in uptake or on the efficacy of ablation. With respect to the tracer dose, Muratet et al.[17] showed differences in the ablation of thyroid remnants (ablative dose of 100 mCi) when using a tracer dose of 1 and 3 mCi (76 and 50% of success, respectively) and Park et al.[15] showed reduced activity on posttreatment (100–200 mCi iodine-131) scans compared to DxSCANS in 40% of patients given 3 mCi, 67% with 5 mCi and 89% with 10 mCi. McDougall et al.[21] did not detect stunning with a dose of 2 mCi. This effect can be prevented at 5 mCi when the ablative dose is administered within < 4 days.[22,23] In the present study, a tracer dose of 5 mCi and an interval of 72 or 3 months between the diagnostic scan and treatment were employed, considering that the stunning effect was demonstrable when the interval was more that a week.[14,16] We emphasize that our patients received a high dose of iodine-131 for ablation of cervical remnants (100 mCi) and the elevated efficacy of this treatment might have minimized the stunning effect, with doubts remaining regarding the occurrence of significant repercussions when low doses are applied. However, the similar success obtained with the treatment of distant metastases (with and without diagnostic scanning) does not support this hypothesis.[23]

Thyroid bed uptake was observed in some patients (< 0.5% of all cases) despite the presence of Tg levels < 2 ng/m*l* and the absence of apparent disease by others methods. The present study is in agreement with others reports in the literature.[13,36] Cailleux et al.[13] observed cervical uptake in 15/210 patients with Tg levels off T4 < 1 ng/m*l* and Pacini et al.,[36] studying 315 patients with undetectable stimulated Tg by whole-body scanning, observed cervical uptake in 28.6% of cases, with the patients showing no evidence of disease and good evolution without the need for ablative therapy. Undetectable or low stimulated thyroglobulin is a more specific criterion for the assessment of initial treatment than scan in low risk patients. The control WBS was negative in the large majority and positive in the thyroid bed in a small minority.

The possibility that thyroid bed uptake may be due to residual or recurrent tumor is always considered. However, we do not recommend iodine-131 therapy in patients with uptake in the thyroid bed, stimulated Tg < 2 ng/m*l* and negative US neck, in agreement with other authors.[13,36] In the subsequent follow-up, < 1% of these patients with undetectable stimulated Tg experienced recurrent disease.[13,36]

In conclusion, we do not recommend follow-up diagnostic scan in low risk patients with stimulated Tg < 2 ng/m*l* after initial therapy. However, for thyroid cancer survivors who are not at low risk, we advise both scan and a stimulated Tg. Tg is a not a sufficient test for high risk patients.[37]

We verified that the 100 mCi dose is efficient in the ablation of thyroid remnants, especially when cervical uptake is < 2%. Stunning does not occur when treatment is initiated within 72 h or 3 months after diagnostic scan. Tg better differentiates patients with and without evidence of disease than follow-up diagnostic scan, that can be avoided in low risk patients with stimulated Tg < 2 ng/m*l*.

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