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5mCi Pretreatment Scanning Does Not Cause Stunning When the Ablative Dose is Administered Within 72 Hours

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ABSTRACT

Objective: To determine the stunning effect of a tracer dose of 5mCi iodine-131. **Patients and Methods:** We retrospectively analyzed 145 patients who received the first ablative treatment at our service. Patients were divided according to disease status determined upon post-treatment scanning (101 patients with thyroid remnants and 44 with pulmonary metastases) and whole-body scanning before ablation (performed on 69 individuals). All patients with thyroid remnants were treated with an ablative dose of 100mCi and those with metastases received 200mCi. **Results:** In patients with remnants only (n= 41) or metastases (n= 28) submitted to diagnostic scanning, uptake was found to be apparently increased in most patientscases (71 and 73%, respectively) 7 days after therapy, while reduced uptake (visual) was not observed in any patient. The efficacy of ablation was similar in the groups submitted or not to diagnostic scanning: 71 and 80% in patients without metastases (p= 0.28), respectively, and 43 and 50% in those with pulmonary involvement (p= 0.64). **Conclusion:** The present results indicate that diagnostic scanning using a 5mCi iodine-131 dose does not interfere with uptake of the ablative dose or with treatment efficacy when ablation is performed within 72h. **(Arq Bras Endocrinol Metab 2005;49/3:420-424)**

Keywords: Scanning; Stunning; Thyroid carcinoma

RESUMO

Rastreamento Prévio Com 5mCi Não Causa Interferência Quando a Dose Ablativa é Administrada Dentro de 72 Horas.

Objetivo: Determinar a interferência de uma dose traçadora de 5mCi de ^{131}I. **Pacientes e Método:** Nós analisamos retrospectivamente 145 pacientes que receberam o primeiro tratamento ablativo em nosso serviço. Eles foram divididos de acordo com o estadio da doença determinado pelo rastreamento pós-terapêutico (101 pacientes com remanescentes tireoidianos e 44 com metástases pulmonares) e *scanning* de corpo inteiro antes da ablação (realizada em 69 indivíduos). Todos os pacientes com remanescentes tireoidianos foram tratados com uma dose ablativa de 100mCi e aqueles com metástases receberam 200mCi. **Resultados:** Nos pacientes com remanescentes apenas (n= 41) ou metastases (n= 28) submetidos ao *scanning* diagnóstico, a captação encontrava-se aparentemente aumentada na maioria dos patientscasos (71 e 73%, respectivamente) 7 dias após a terapia, enquanto captação reduzida (visual) não foi observada em nenhum paciente. A eficácia da ablação foi similar nos grupos submetidos ou não ao rastreamento diagnóstico: 71 e 80% em pacientes sem metástases (p= 0,28), respectivamente, e 43 e 50% naqueles com envolvimento pulmonar (p= 0,64). **Conclusão:** Esses resultados indicam que o rastreamento diagnóstico usando uma dose de 5mCi de ^{131}I não interefere com a captação da dose ablativa ou com a eficácia do tratamento quando a ablação é realizada dentro de 72h. **(Arq Bras Endocrinol Metab 2005;49/3:420-424)**

Descritores: Rastreamento; Interferência; Carcinoma de tireóide

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THE ABLATIVE IODINE-131 dose to be administered in the initial treatment of differentiated thyroid carcinoma (1-3) depends on factors such as the presence of lymph node or distant metastases (3-5), remnant tissue masses in the thyroid bed (6,7), and the capacity of the cell to take up iodine (4,7). Therefore, assessment before administration of the ablative dose is recommended, especially in the case of high risk patients in order to diagnose metastases and to determine the sensitivity of the tissue to iodine, thus contributing to the definition of the ablative dose.

However, the administration of a tracer dose of iodine to thyroid cells might compromise their function, including iodine uptake, and therefore markedly reduce the efficacy of the therapeutic dose. This phenomenon, called stunning effect, does not seem to occur when treatment is performed less than 5 days after diagnostic scanning (8-10), or when the diagnostic iodine-131 dose administered does not exceed 2mCi (10,11), a less sensitive dose (12).

The lack or decrease of iodine uptake on post-treatment scans suggests the occurrence of the stunning effect (9,10,13-16), but other parameters should also be taken into account, mainly the efficacy of ablation which is the main end-point (8,9,11,14,16-18).

At present, routine diagnostic iodine scanning is rare in many services due to its limited sensitivity especially when low doses are employed (12), the risk of stunning, and the excellent efficacy obtained with the high doses employed in ablative therapy (19,20). However, selected cases (patients at high risk of metastases) require iodine scanning assessment, and in these patients stunning represents the limiting factor.

The objective of the present study was to determine the occurrence of stunning after scanning with 5 mCi iodine-131, followed by ablative treatment 72 h later, by comparing pre- and post-treatment iodine uptake (visual) and by assessing the efficacy of ablation in patients submitted or not to pretreatment scanning.

PATIENTS AND METHODS

We retrospectively analyzed patients seen at the Santa Casa Nuclear Medicine Service, Belo Horizonte, Brazil, for ablative treatment with iodine-131 during the period from 2000 to 2003 and selected cases (by post-treatment scanning) with thyroid remnants only who received 100mCi or cases with diffuse and bilateral pulmonary metastases without other distant metastases who received 200mCi iodine-131, submitted or not to pretreatment scanning. Included in the study were 145 patients (16 men and 129 women) ranging in age from 11 to 76 years (mean ± SD, 41.4 ± 23) with differentiated thyroid carcinoma (109 with papillary carcinoma, 31 with follicular carcinoma and 5 with Hürthle cell carcinoma) submitted to total thyroidectomy. The protocol was approved by the Research Ethics Committee of the institution.

The patients were divided into four groups according to the following criteria: patients presenting only thyroid remnants who received 100mCi iodine-131 and who were submitted (group 1, n= 41) or not (group 2, n= 60) to pretreatment scanning; patients with diffuse and bilateral pulmonary metastases who received 200mCi iodine-131 and who were submitted (group 3, n= 28) or not (group 4, n= 16) to pretreatment scanning. The patients of groups 1 and 2 (with thyroid remnants only) and of groups 3 and 4 (with pulmonary metastases) were similar in terms of gender, age and stage of the disease.

The stunning effect was determined in two ways: by comparing pre- and post-treatment cervical or pulmonary uptake (visual) in the groups submitted to diagnostic scanning before treatment, and by comparing the efficacy of ablation in patients submitted or not to diagnostic scanning assessed by iodine scanning and by the determination of thyroglobulin (Tg) levels after T4 withdrawal 6 months to one year after treatment and defined as stimulated Tg< 2ng/ml (in patients without anti-thyroglobulin antibodies) and a clean whole-body scan.

Thyroglobulin and anti-thyroglobulin antibody measurements

Tg was measured withby an immunoradiometric assay (ELSA - hTG, CIS Bio International, France) with a functional sensitivity of 0.8ng/ml, intra-assay precision of 2.4-6.6% and interassay precision of 5.1-8%, with the reference value established by the laboratory being 3 to 42ng/ml. All patients showed TSH levels >30 mIU/l after withdrawal of T4 for 4 weeks. Anti-thyroglobulin antibodies (TgAb) were determined by a chemiluminescent assay (Chemiluminescent ICMA, Nichols Institute Diagnostics, San Juan Capistrano, CA) with a detection limit of 1 IU/ml and intra- and interassay precision of 8.7 and 5.9%, respectively, for values of 2 to 40 IU/ml. Tg measurement was considered only when TgAb was undetectable.

Imaging methods

Diagnostic scanning was performed with a tracer dose of 5mCi iodine-131 during hypothyroidism after T4 withdrawal for 5 weeks and administration of a low iodine diet during the 2 weeks preceding the exam. Whole-body images were obtained 72h after iodine administration. Post-treatment 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 similar and conformed with National Electrical Manufacturers Association (NEMA) specifications. Whole-body scans were performed at a scan speed of 10cm / min using a step and shoot mode with body contour option. Both anterior and posterior views were obtained, as well as spot views at 15min / view. Uptake upon scanning was analyzed visually by three experienced nuclear medicine professionals. Other imaging methods used for the definition ofthe disease status were cervical ultrasound, contrast-free chest and mediastinum computed tomography and radiography, bone radiography, and Sestamibi scanning.

Statistical methods

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

RESULTS

Among the patients with cervical remnants who were submitted to pretreatment scanning (group 1), uptake was apparently more intense upon post-treatment scanning in 30 / 41 cases (71%) and was unchanged in the remaining 11 patients, while no ornone of the patients studied presented less intense or no uptakewas observed in anyof the patients studied . In the group of patients with pulmonary metastases (group 3), post-treatment scanning also confirmed all pretreatment cases and uptake apparently increased in 20 / 28 patients (73%) and remained unchanged in 8, while none of the patients showed reduced uptake.

Six months to one year after treatment, 30 / 41 (71%) of the patients submitted to pretreatment scanning and without metastases (group 1) were apparently free of the disease (stimulated Tg< 2 ng / ml and no uptake on control scans). No significant difference in treatment efficacy was observed between patients with increased uptake after ablation (73.3%) and those with unchanged uptake (72.7%) (p= 0.72). Treatment was efficient in 48 / 60 (80%) patients empirically treated with 100mCi radioiodine and not submitted to scanning prior to ablation (group 2), with no significant difference between patients submitted or not to pretreatment scanning (p= 0.28).

In the case of patients with pulmonary metastases, efficacy also did not differ between patients submitted (group 3) or not (group 4) to pretreatment scanning (43 and 50%, p= 0.64). Increased uptake was not associated with greater treatment efficacy (45 and 37.5%, p= 0.95).

DISCUSSION

The real frequency and the impact of the stunning effect on the ablative treatment of thyroid remnants continue to be poorly defined. Differences between studies impair definitive conclusions, including variations in the dose used for diagnostic scanning, the interval between this exam and treatment, the therapeutic dose prescribed, time of post-treatment scanning, and the definition of this phenomenon itself which might be based only on the reduction in uptake or on the efficacy of ablation, the latter being defined on the basis of various criteria.

With respect to the tracer dose, Jeevanram et al. (21) observed a negative correlation between the calculated radiation dose delivered to the thyroid bed and the dose predicted by calculations involving initial (diagnostic) radioiodine uptake (diagnostic dose ranging from 3.7 to 185 MBq). Park et al. (13) showed reduced activity on post-treatment (100-200mCi iodine-131) scans compared to DxSCANS in 40% of patients treated with 3mCi, 67% treated with 5mCi and 89% treated with 10mCi. Muratet et al. (11) showed differences in the ablation of thyroid remnants (ablative dose of 100 mCi) when using a tracer dose of 1 and 3mCi (76 and 50% of success, respectively), and McDougall et al. (10) did not detect stunning with a dose of 2mCi (only 1.4% of patients showed reduced therapeutic uptake).

The interval between the diagnostic scan and treatment also plays an important role, with no stunning effect being observed when this interval was less than 5 days (8-10), while stunning was demonstrated when treatment was initiated after one week (15-17). Park et al. (13) obtained discordant outcomes and observed stunning when the time between diagnostic scanning and the therapeutic dose ranged from hours to days, but performed post-treatment scanning within 24-48h after the ablative dose, preventing adequate visualization of thyroid remnants due to extremely high background activity (8).

We emphasize that our patients received a high dose of iodine-131 (100mCi) for ablation of cervical remnants, and the high efficacy of this treatment might have minimized the stunning effect, but doubts remain whether low doses would have significant repercussions. However, the similar success obtained in our study with the treatment of distant metastases (with and without diagnostic scanning) does not support this hypothesis, in agreement with the results previously published by Morris et al. (8).

Whole-body scans obtained 7 days after treatment reveal substantially more lesions than scans performed 2 days after treatment as a result of the background ratio (22); however, this finding may contribute to, but does not explain alone, the different results reported in the literature. This may explain the higher uptake found on post-treatment scans in 70% of our patients.

Although stunning can be suspected to be responsible for the difference between pre- and post-treatment uptake (9,10,13-16), treatment efficacy seems to be the fundamental parameter in the definition of the impact of this phenomenon which, however, has not been considered in all studies. Morris et al. (8) did not observe differences in the success of ablative therapy between patients submitted or not to pretreatment scanning with 5mCi iodine-131 (64.9 and 66.7%, respectively). Park et al. (18) obtained 60 and 75% success rates (100-200mCi iodine-131) using 3-10mCi iodine-131 and 300µCi iodine-123, respectively, and Muratet et al. (11) demonstrated an efficacy of 50 and 76% with 3 and 1mCi 131-iodine (ablative dose – 100mCi), respectively.

In the present study, the efficacy of ablation was defined as a clean scan after administration of 5mCi iodine-131 and stimulated Tg levels < 2ng/ml. However, different success rates for ablation of thyroid remnants can be explained, in part, by the various criteria adopted to determine treatment efficacy, such as a negative 3mCi scan (11), a negative 5mCi scan (17), a negative 3-10mCi scan (18) and clean scans and Tg levels < 3 ng/ml (16) and < 1 ng/ml (20).

The impact of treatment seems to be greater on metastases than on thyroid remnants (15), but in the present study no difference in the effectiveness of radioiodine was observed even in patients with pulmonary involvement, in agreement with Morris et al. (8).

Our results are in agreement with a recent and ampleextensive review published by Morris et al. (23), who concluded that there is no convincing evidence regarding the true occurrence of the stunning effect, with the authors considering exactly the same points as discussed at the beginning of this section: dose used for diagnostic scanning, the interval between this exam and treatment, the therapeutic dose prescribed, time of post-treatment scanning, efficacy of ablation, and how success of ablation is determined. The most important aspect of that review is the lack of studies that clearly demonstrate a negative impact of diagnostic scanning on the success of ablative treatment, reported only by Muratet et al. (11). The considerations made by Morris et al. (23) go beyond and consider the possibility of some ablative effect of the diagnostic tracer dose as proposed in another investigation (16).

CONCLUSION

The present results suggest that pretreatment iodine-131 scanning (5mCi dose) does not reduce uptake of the therapeutic dose and does not compromise the efficacy of ablation of thyroid remnants and distant metastases when treatment is administered 72h after the tracer dose.

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