Extrathyroidal tissue radiation damage from ^{131}I remnant ablation is significantly less with rhTSH preparation than with thyroid hormone withdrawal

Rosario PW, Borges MA, Purisch S. Preparation with recombinant human thyroid-stimulating hormone for thyroid remnant ablation with ^{131}I is associated with lowered radiotoxicity. J Nucl Med 2008;49:1776-82.

SUMMARY

BACKGROUND Preparation for ^{131}I remnant ablation using recombinant human thyrotropin (rhTSH) in patients with differentiated thyroid cancer results in lower extrathyroidal radiation than occurs in patients prepared by thyroid hormone withdrawal (THW). However, there are no studies that directly demonstrate differences in tissue damage using the two forms of preparation. This is a retrospective study aimed at comparing the damage caused by remnant ablation when patients receive one or the other form of preparation.

METHODS The study subjects were consecutive patients with papillary thyroid cancer (PTC) or follicular thyroid cancer (FTC) who underwent total thyroidectomy and remnant ablation with 100 mCi (3.7 MBq) of ^{131}I from August 2003 through December 2006. Damage to salivary glands and ovaries and testes, hematologic damage, and oxidative injury were evaluated. The serum amylase for salivary gland studies were obtained before and 48 hours after ^{131}I; and salivary pain was evaluated at 2 and 7 days after ^{131}I. Follicle-stimulating hormone (FSH) was measured immediately before and 6 months after ^{131}I in both men and women. A complete blood count was performed immediately before and 30, 45, and 60 days after ^{131}I. Plasma 8-epi-prostaglandin F2α (PGF2α), a marker of dose-dependent in vivo oxidation injury, was measured immediately before and 4 days after ^{131}I therapy. Patients were divided into two groups, one that received rhTSH (group A) and another that underwent THW (group B) in preparation of remnant ablation.

RESULTS A total of 94 patients with PTC or FTC were enrolled in the study, 30 in group A, and 64 in group B; 64 were female (47%) and 30 male (21%), with a mean (±SD) age of 45±9.5 and 44±11 years, respectively. There were no significant differences in tumor histology, size, or extrathyroidal invasion or the interval between thyroidectomy and remnant ablation in the two groups; however, the serum TSH level immediately before the administration of ^{131}I was 118±28.5 μIU/ml in group A and 85±23 in group B (P<0.05). Uptake of ^{131}I was no more than 2% in any patient. In groups A and B, serum FSH was elevated 105% and 236% in men, and 65% and 125% in women, in the groups A and B, respectively (P<0.001, Figure 1). In groups A and B, amylase was elevated 48 hours after ^{131}I in 36.6% and 80% (P<0.001) of the patients, and symptoms of acute sialoadenitis occurred in 30% and 58.3% (P = 0.01, Figure 1). Thrombocytopenia (<1000,000/mm^3) or neutropenia (<1500/mm3) (lowest count) occurred up to 60 days after ^{131}I in 7% of group A and 21.4% of group B (P = 0.01). The mean decrease (lowest count) of neutrophils was 20% and 45%, and the mean decrease in platelets was 25% and 52% (P<0.01 for both). The increase in plasma 8-epi-PGF2α was 56% and 100%, and the mean increase was 60% and 125%. (Figure 2)

After a follow-up of approximately 2 to 5 years, FSH was normal in 20 of 27 patients (74%) who had elevated levels of FSH after ablation, and platelet and neutrophil counts returned to normal in 10 of 12 (83%) with early neutropenia or thrombocytopenia.

CONCLUSION Extrathyroidal tissue radiation damage from ^{131}I remnant ablation is significantly less with rhTSH preparation than with thyroid hormone withdrawal.

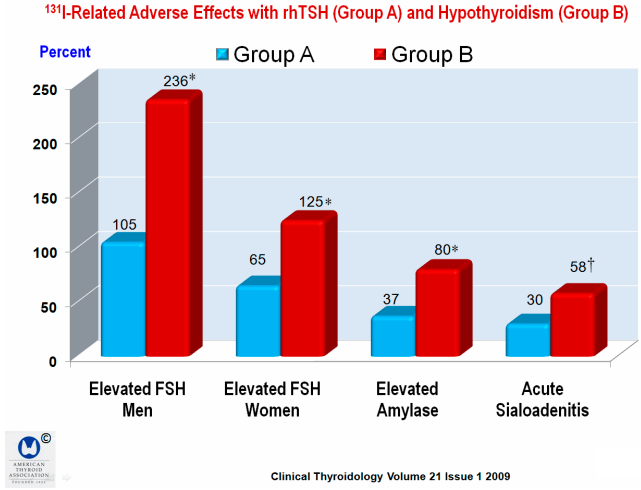

Figure 1. The adverse effects of ^{131}I on gonads and salivary glands are greater in patients prepared with rhTSH (group A) than in those prepared with thyroid hormone withdrawal (group B). *P = 0.001. †P = 0.01. This figure was drawn from the data in Table 4 by Rosario et al.

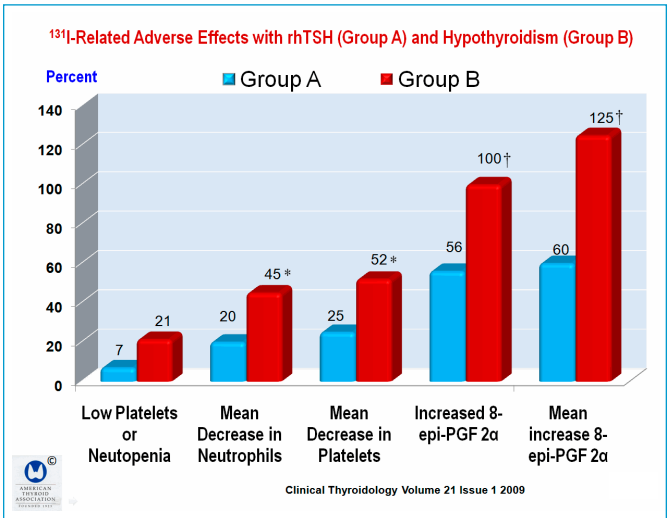

Figure 2. The adverse effects of ^{131}I on bone marrow and oxidative tissue damage (epi-prostaglandin F2α [PGF2α]). Thrombocytopenia or neutropenia was observed 30, 45, and 60 d after ^{131}I administration in 4, 8, and 2 patients, respectively. Mean decrease in neutrophils and platelets is the lowest count. Lowest platelet count was observed 30, 45, and 60 days after ablation in 20, 44, and 20 patients, respectively. Lowest neutrophil count was observed 30, 45, and 60 days after ablation in 16, 40, and 28 patients, respectively. *P <0.01, †P<0.001. This figure was drawn from the data in Table 4 by Rosario et al.

COMMENTARY

This study directly compares the tissue injury caused by 100 mCi (3.7 GBq) of ^{131}I administered for remnant ablation in patients prepared with rhTSH as compared with THW. The differences in injury caused by the two types of preparation are impressive. In all, six of the seven patients who continued to show elevated FSH levels and the two patients with persistent hematologic abnormalities were in group B. Hyperamylasemia persisted in only two patients, also from group B, and recurrent or persistent pain or xerostomia was observed in four patients, one from group A and three from group B, all of whom showed elevated amylase levels or acute sialoadenitis after ablation.

There is robust evidence that the mean effective half-life of ^{131}I is shorter by 31% in euthyroid patients treated with rhTSH as compared with that in hypothyroid patients undergoing THW (1-3). This significantly decreases the radiation doses delivered to extrathyroidal tissues. Combined with smaller amounts of ^{131}I, in the range of 30 mCi, the amount of whole-body radiation delivered by ^{131}I for remnant ablation can be substantially reduced. The ATA guidelines suggest that the minimum ^{131}I activity (30 to 100 mCi) necessary to achieve successful remnant ablation should be used, particularly for low-risk patients (4). This recommendation is based on the fact that ^{131}I activities between 30 and 100 mCi generally show similar rates of successful remnant ablation (5-10). Also, recurrence rates are comparable following THW and rhTSH preparation (11). These data directly imply that 30 mCi is the preferred amount of ^{131}I for patients at low risk of adverse outcomes. This study by Rosario et al. adds one more piece of evidence to support the notion that the smallest amount of ^{131}I in patients prepared with rhTSH is likely to provide the lowest risk of nonthyroidal tissue injury.

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References

1. Pacini F, Ladenson PW, Schlumberger M, et al. Radioiodine ablation of thyroid remnants after preparation with recombinant human thyrotropin in differentiated thyroid carcinoma: results of an international, randomized, controlled study. J Clin Endocrinol Metab 2006;91:926-32.

2. Remy H, Borget I, Leboulleux S, et al. ^{131}I effective half-life and dosimetry in thyroid cancer patients. J Nucl Med 2008;49:1445-50.

3. Hänscheid H, Lassmann M, Luster M, et al. Iodine biokinetics and dosimetry in radioiodine therapy of thyroid cancer: procedures and results of a prospective international controlled study of ablation after rhTSH or hormone withdrawal. J Nucl Med 2006;47:648-54.

4. Cooper DS, Doherty GM, Haugen BR, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2006;16:109-42.

5. Rosario PW, Reis JS, Barroso AL, et al. Efficacy of low and high ^{131}I doses for thyroid remnant ablation in patients with differentiated thyroid carcinoma based on post-operative cervical uptake. Nucl Med Commun 2004;25:1077-81.

6. Pilli T, Brianzoni E, Capoccetti F, et al. A comparison of 1850 (50 mCi) and 3700 MBq (100 mCi) 131-iodine administered doses for recombinant TSH-stimulated postoperative thyroid remnant ablation in differentiated thyroid cancer. J Clin Endocrinol Metab 2007;92:3542-6.

7. Bal C, Padhy AK, Jana S, et al. Prospective randomized clinical trial to evaluate the optimal dose of 131 I for remnant ablation in patients with differentiated thyroid carcinoma. Cancer 1996;77:2574-80.

8. Bal CS, Kumar A, Pant GS. Radioiodine dose for remnant ablation in differentiated thyroid carcinoma: a randomized clinical trial in 509 patients. J Clin Endocrinol Metab 2004;89:1666-73.

9. Mazzaferri EL. Thyroid remnant ^{131}I ablation for papillary and follicular thyroid carcinoma. Thyroid 1997;7:265-71.

10. Mäenpää HO, Heikkonen J, Vaalavirta L, et al. Low vs. high radioiodine activity to ablate the thyroid after thyroidectomy for cancer: a randomized study. PLoS ONE 2008;3:e1885.

11. Tuttle RM, Brokhin M, Omry G, et al. Recombinant human TSH-assisted radioactive iodine remnant ablation achieves short-term clinical recurrence rates similar to those of traditional thyroid hormone withdrawal. J Nucl Med 2008;49:764-70.