

# Before Moving Towards Recombinant Thyrotropin, Can We Benefit From Anti-Thyroid Drugs? A Case Study

Soltani A<sup>a</sup>, Rahimian N<sup>b</sup>, Rahbar Z<sup>b</sup>, Moosapour H<sup>a</sup>

<sup>a</sup>Endocrinology & Metabolism Research Centre, Shariati Hospital and <sup>b</sup> Students Scientific Research Center, Tehran University of Medical Sciences, Tehran, I. R. Iran

**I**n patients with thyroid papillary carcinoma, performing an effective radioactive iodine ablation after total thyroidectomy requires adequate levels of serum thyrotropin. Administration of recombinant human thyroid stimulating hormone (rhTSH) is the current established method for patients with insufficient serum TSH levels four to six weeks after surgery and levothyroxine discontinuation. Two major problems with rhTSH are its cost and availability in most countries worldwide. We have used propylthiouracil (PTU), a routine anti-thyroid drug, for the first time to induce a TSH rise. Our patient was a 33-year-old woman with remnant thyroid tissue of 11.5×4 mm after thyroidectomy. Her TSH was 12.7 µIU/ml, five weeks after surgery, and rose to 30.0 µIU/ml after a 10 day trial of PTU. Radioiodine uptake index also increased from 28% to 56%. Radioiodine ablation was successfully done and patient showed no sign of recurrence or metastasis after 4 years. We propose that anti-thyroid drugs may be considered for post-operative induction of TSH rise in patients considered for radioiodine ablation of thyroid cancer. This may increase the chance of successful ablations with least possible cost.

**Key Words:** Thyroid papillary carcinoma, Iodine radioisotopes, Anti-thyroid drugs, Recombinant thyrotropin

*Correspondence:* Akbar Soltani, MD, Endocrinology and Metabolism Research Centre, fifth floor, Shariati Hospital, Northern Kargar Ave, Tehran 14114, Iran  
E-mail: soltania@sina.tums.ac.ir

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## Introduction

Total thyroidectomy and subsequent radioactive iodine ablation of the remnant thyroid tissue is the established treatment for papillary thyroid carcinoma.<sup>1-4</sup> Prerequisite for a successful ablation is high levels of TSH and radioactive iodine uptake (RAIU) index. This is usually achieved by discontinuation of levothyroxine after thyroidectomy for four to six weeks. In some patients, however, TSH and RAIU levels may not rise sufficiently, which occurs especially after near-total thyroidectomy. In this situation, administration of recombinant human TSH (rhTSH) [or Thyrogen®] has been proposed as the method of choice to increase the chance successful ablation.<sup>3,5</sup> Concerning cost and availability of rhTSH, its use is limited in most of clinical settings and many physicians are compelled to start radioiodine ablation without sufficient uptake. Here we report a case with scarce TSH rise after surgery who responded well to an anti-thyroid drug.

## Materials and Methods

The patient was a 33-year-old woman with papillary thyroid carcinoma diagnosed, in August 2004. The tumor was 2×2 cm and in stage I according to TNM classification system (with tumor extending beyond thyroid capsule, metastases to paratracheal lymph nodes, and no distant metastasis). Given apparent adhesions to recurrent laryngeal nerve, she underwent near-total thyroidectomy in September 2004; the post-surgery whole body <sup>131</sup>I scan showed an uptake in the thyroid bed and in the neck ultrasonography, a remnant tissue of 11. 5×4 mm was detected and radioiodine ablation was considered for the patient.

The optimum level of serum TSH for iodine ablation is higher than 25 μIU/ml.<sup>1</sup> To induce TSH rise, levothyroxine was discontinued for the patient and she went on a low iodine diet two weeks after discontinuation (for three weeks). The serum TSH did not rise sufficiently in this period and reached 12.7 μIU/ml five weeks after levothyroxine discontinuation. Her RAIU index was 28% at the time. The therapeutic situation was described for the patient and she agreed to collaborate in this novel study and signed the informed consent. Propylthiouracil (PTU) was prescribed in dosage of 200 mg, 3 times daily for 10 days. She was on low-iodine diet in this period. Four days after termination of PTU, serum TSH reached to 30. 0 μIU/ml and RAIU index rose to 56%. She received 150 mCi of <sup>131</sup>I for the ablation of remnant tissue.

The patient reported no sign of hypothyroidism or any side effects during PTU therapy, and was followed up for 4 years. The whole body <sup>131</sup>I scan six months later and thyroglobulin measurements at 6, 12, 18, and 48 months after ablation showed no recurrence or metastases. Neck ultrasonography and TPO-antibody serum levels are normal, as well; the patient has no complaints and is reported to be well in her physical examination reports.

## Discussion

In a sensitive search on MEDLINE and EMBASE, there was no study suggesting anti-thyroid drugs as a means for induction for more successful ablation in post-surgical management of thyroid cancer. This report presents the first study that proposes PTU as an alternative to rhTSH in order to increase efficacy of radioiodine ablation in thyroid carcinoma.

<sup>131</sup>I is administered post-operatively for three reasons: To destroy normal thyroid remnants, to increase the sensitivity of whole body scanning and specificity of serum thyroglobulin measurements, and, finally, to destroy occult metastases or microscopic carcinoma.<sup>2</sup> However, in order to perform an effective radioiodine ablation, serum TSH concentrations should be above 25-30 μIU/ml to push <sup>131</sup>I into the neoplastic remnant tissue.<sup>1,2,7</sup> A thyroidectomy done by an “experienced” surgeon, makes follow up exam be much easier. A near-total thyroidectomy would minimize the chance for a high uptake requiring other interventions.

The usual way to induce TSH rise is post-operative withdrawal of levothyroxine for at least 4 to 6 weeks.<sup>7</sup> Depletion of the T3 and T4 source stimulates the hypothalamic-pituitary-thyroid axis and a rise in serum TSH level results. If the TSH level does not reach the optimal level by this method, rhTSH administration (0. 9 mg intramuscular injection for two consecutive days) is the recommended approach.<sup>1,8,9</sup> Moreover, some clinicians prefer to prescribe rhTSH primarily as levothyroxine treatment needs not to be discontinued and hypothyroidisms signs are minimal.

However, the two major problems with rhTSH are its availability and cost. The drug is not available in many clinical settings throughout the world and a single dose costs between 1300\$ and 1600\$ for each patient in the US;<sup>10</sup> this means that many patients across the world undergo radioiodine ablation without appropriate preparation. Given these constraints, a great demand is perceived

for an alternative way to induce serum TSH rise. According to the concept that the remnant tissue may secrete thyroid hormone, and because anti-thyroid drugs seem to be safer and more effective, we decided to administer an anti-thyroid drug for this patient.

Of the two most commonly used anti-thyroid drugs, PTU and methimazole, both are effective at decreasing T<sub>4</sub> and T<sub>3</sub> synthesis but PTU half-life is shorter and its intra-thyroidal concentration is lower than methimazole. Hence, it may be washed out more quickly and this facilitates absorption of radioiodine. Given this background, we chose to prescribe PTU in our patient. The administration of <sup>131</sup>I was postponed to four days after discontinuation of PTU. This 4-day interval is approximately equal to the 3 to 5 day intra-thyroidal PTU half-life and is necessary

to reduce the inhibitory effect of PTU on thyroïdal uptake. 1

In conclusion, for better surgical approach for easier follow up and because rhTSH is costly, T<sub>4</sub> withdrawal could be the standard approach; however in patients with remnant thyroid tissue and insufficient TSH and RAIU index for effective radioiodine ablation, administration of safe and available anti-thyroid drugs may induce TSH rise and improve the prognosis of treatment. This may also shorten the time needed for levothyroxine discontinuation and associated hypothyroidism. These results, however, need verification in future prospective studies.

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