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Use of Recombinant Human TSH (RH TSH, Thyrogen®) in Differentiated Thyroid Carcinoma

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DESCRIPTION

Recombinant human TSH (rhTSH, Thyrogen®) has become a standard preparation for RAI in thyroid cancer management in many countries over the last 20 years. In 2012 the ESTIMABL study demonstrated equivalence of rhTSH and low dose (30 mCi) 131 I ablation to thyroid hormone withdrawal and high dose (100 mCi) ablation in low-to-intermediate risk differentiated thyroid carcinoma, as did the simultaneously published HiLo study [1]. Subsequent follow-up of the ESTIMABL cohort showed disease recurrence was not related to ablation strategy. Similarly, it has been found that post-surgical ablation with high or low RAI activity results in similar disease recurrence outcomes in intermediate risk differentiated thyroid carcinoma.

In 2009 we published our early use (1999-2006) of rhTSH in thyroid cancer follow-up. In this retrospective study of 90 patients, rhTSH was used for 96 diagnostic episodes and for 18 episodes to facilitate treatment with 131 I [2]. There were 70 cases of papillary thyroid carcinoma, 16 of which were follicular-variant papillary thyroid carcinomas, 17 follicular thyroid carcinomas and 3 Hurthle cell carcinomas [3]. Twenty-six patients had stage I cancer, 16 stage II, 23 stage III, 20 stage IV and 5 were unclassifiable because of incomplete records of surgical notes and histopathology [4]. Most patients (63) were considered to have good-prognosis cancers and hence unlikely to require thyroid hormone withdrawal for 131 I therapy [5]. Fifteen patients received rhTSH for other reasons related to an advanced stage of cancer and other comorbidities that would have made thyroxine withdrawal debilitating, or to facilitate 131 I therapy in patients where TSH failed to rise to more than 30 m µ /L despite thyroxine withdrawal [6].

In stages I and II cancer (n=42), of three patients with stimulated thyroglobulin (Tg) 1–2 µ g/L, none had identifiable disease, and the three patients who had stimulated Tg>2 µ g/L, did not experience recurrent disease during follow up. In contrast, in stages III and IV cancer (n=43) 2 of 5 with stimulated Tg 1-2 µ g/L, had identifiable disease and 7 of 10 with stimulated Tg>2 µ g/L, had identifiable disease [7]. In Tg-positive, WBS-negative disease, further imaging identified persistent/recurrent disease [8].

We concluded that rhTSH was effective and safe in the management of thyroid cancer follow up for diagnosis of persistent/recurrent cancer and to enable 131 I treatment [9]. In no case did rhTSH-stimulated whole body 131 I scanning identify the presence of disease not also identified by raise basal Tg or stimulated Tg. Therefore, we suggested that in low-risk cancer WBS may be omitted [10].

Our findings supported the efficacy and safety of rhTSH for diagnostic and therapeutic purposes, and the recommendation in the then current management guidelines of the ATA that low-risk patients with negative stimulated Tg do not require routine diagnostic WBS during follow up [11]. In low-risk thyroid cancer, we suggested that WBS may be omitted in favour of using stimulated Tg values, and that in low-risk patients who are clinically free of disease, with undetectable serum Tg on suppressive thyroxine therapy, if high-quality neck ultrasonography shows no disease then rhTSH stimulation may not be necessary, as had been indicated by findings of Smallridge, et al. using a high-sensitivity Tg assay, that a Tg level <0.1 µ g/L, during TSH suppression was predictive of a stimulated Tg of <2 µ g/L [7]. We therefore foreshadowed that the availability of sensitive Tg assays that have a functional sensitivity of 0.1 µ g/L, would preclude the need for TSH stimulation when evaluating patients for persistent or recurrent cancer, as has indeed come to pass as standard management [12]. Furthermore, we now know that low and intermediate risk patients with papillary thyroid carcinoma and negative neck ultrasonography (US) and unstimulated Tg<1 µ g/L, at 1-year follow-up can be followed safely by clinical assessment and serum Tg, only requiring US if Tg increases.

Subsequently, we showed that in the setting of 131 I ablation therapy or diagnostic 131 I scanning, a significant proportion of patients (20.2% and 8.3%, respectively) had residual tissue on whole-body scanning despite a negative stimulated serum Tg level. A significant proportion of patients exhibiting this phenomenon (30/39 in the post-ablative 131 I therapy group and 9/10 in the diagnostic I-131 group) had 131 I uptake only in the thyroid bed, likely representing residual benign normal thyroid remnant tissue in most of these cases Kim, et al. reported that a significant proportion of patients with residual 131 I uptake on follow-up diagnostic scanning had spontaneous disappearance of residual 131 I activity (and normalization of serum Tg levels) on subsequent scanning, indicating a benign origin [10]. We also showed that, using SPECT-CT scanning after 131 I ablation, thyroglossal tract thyroid tissue was present in 39/83 (47%; 95% CI: 36%–58%) patients on SPECT/CT. In these 39 patients, this tissue contributed to a significant amount of total neck activity (median=50%; IQR 19%–74%).

Apart from directly assisting in thyroid cancer management, routine use of rhTSH has facilitated efficient use of hospital isolation rooms for radiation protection. Another compelling reason to use rhTSH is to maintain quality of life and the ability to work of the recipient, and to promote compliance with thyroid cancer follow-up protocols [13]. Hypothyroidism after thyroxine withdrawal is often associated with a significant decline in quality of life that is abrogated by rhTSH use, and this can translate into the community cost of rhTSH being offset by the patient's ability to remain working normally.

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