Thyrotropin Suppressive Therapy in Differentiated Thyroid Cancer

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Differentiated thyroid carcinoma (DTC) is the most frequent endocrine tumor, and its incidence has increased significantly in recent years [1]. Total or near thyroidectomy and radioactive iodine ablation followed by thyroxine suppression of thyrotropin (TSH) is an effective and acceptable therapeutic scheme for most DTC patients [2,3]. The preferred drug of TSH suppressive therapy is levothyroxine (L-T4). L-T4 treatment reduces serum TSH level, thereby inhibiting the growth of residual neoplastic tissue, suppressing serum Tg level and reducing tumor recurrence and progression in DTC patients. However, excessive TSH suppression therapy can induce exogenous subclinical hyperthyroidism that may adversely affect the skeletal [4] and cardiovascular systems [5,6]. All those would affect the quality of life of patients with DTC. So far, there is still no consensus about the optimal serum TSH levels that is required for the initial treatment and follow-up of DTC despite several guidelines recommended the TSH suppressive levels. In high-risk patients who have persistent disease, the American Thyroid Association (ATA) and European Thyroid Association (ETA) recommend that the serum TSH level be kept at <0.1 mU/L. In higher-risk but disease-free patients, the ATA recommends TSH levels be kept at 0.1-0.5 mU/L for 5-10 years, whereas the ETA recommends TSH levels <0.1 mU/L for 3-5 years. In low-risk patients, the initial serum TSH levels should be kept at 0.1-0.5 mU/L in the ATA guidelines and <0.1 mU/L in the ETA guidelines. In low-risk and disease-free patients on follow-up, ATA and ETA both recommend serum TSH level be kept in the low normal range (0.3-2.0 mU/L) [7,8].

In recent years, the concept of TSH-suppressive therapy has gradually changed, which recommends to take into account both the risk of recurrence or progression of DTC and the risk from adverse effects of L-T4 therapy. The risk for recurrence and progression in patients with DTC can be divided into three levels: low, intermediate and high risks, according to the ATA guidelines [7], and a similar assessment of the risk of adverse effects of L-T4 suppressive therapy can be also divided into low, intermediate and high risks, summarized by Biondi and Cooper [9]. This can be called "double-risk-adapted strategy". This approach provided differing TSH suppression levels for both initial treatment (in the 2-3 years after radioiodine treatment at our department) and follow-up. We support the risk-adapted strategy for L-T4 therapy in DTC patients. It is reasonable and constructive.

According to the double-risk-adapted strategy, suggested TSH levels in patient with DTC during follow-up is as follow: In high-risk patients with persistent or metastatic disease, no matter what risk type from L-T4, TSH levels should be kept undetectable (<0.1 mU/L). In high-risk patients and disease free for 5-10 years, no matter what risk type from L-T4, whose serum TSH levels at 0.1-0.5 mU/L should be considered. In those patients with high risk from L-T4, the degree of TSH suppression level should be adapted to the clinical situation. In patients with intermediate risk from L-T4, cardiovascular drugs, calcium, and vitamin D should be considered. In patients with an intermediate risk for cancer recurrence or progression and high or intermediate risk of adverse effects from L-T4, the degree of TSH suppression should be dynamically monitored and modified according to clinical assessment.

After 5-10 years of follow-up if serum Tg is undetectable and there is no clinical evidence of disease, a TSH level of 1.0-2.0 mU/L is advisable. In disease-free low-risk DTC patients during follow-up, the TSH level at 1-2 mU/L is appropriate in patients with high or intermediate risk of adverse effects. In patients with a low risk of adverse effects, the TSH level at the low normal range (0.3-2.0 mU/L) is advisable.

In all, the benefit and the risk of the adverse effects of L-T4 suppressive therapy for DTC patients should be carefully balanced in clinical practice. TSH suppressive level should be modified according to clinical assessment and be individualized against the potential for adverse effects according to the double-risk-adapted strategy for L-T4 suppressive therapy. More aggressive TSH suppression is advisable in patients with high-risk of cancer recurrence or progression, whereas less aggressive TSH suppression is reasonable in low-risk DTC patients.

References

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Received December 21, 2012; Accepted December 26, 2012; Published December 28, 2012

Citation: Xue YL, Qiu ZL, Luo QY (2013) Thyrotropin Suppressive Therapy in Differentiated Thyroid Cancer. Altern Integ Med 2: e106. doi:10.4172/2327-5162.1000e106

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