

The Effect of TSH Suppression Therapy on the Efficacy and Immune Function of Postoperative Patients with Thyroid Cancer

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Abstract: *Objective:* To investigate the efficacy and immune function of thyroid stimulating hormone (TSH) suppression therapy in postoperative thyroid cancer patients. *Methods:* Sixty thyroid cancer patients admitted from July 2020–July 2022 were recruited and randomly divided into two groups. The control group (30 patients) received hormone replacement therapy, while the study group (30 patients) received TSH suppression therapy. The thyroid function, clinical efficacy, immune function, and tumor markers of the two groups were compared. *Results:* After treatment, the levels of free triiodothyronine (FT3) and thyroxine (FT4) in both groups increased significantly, while TSH levels decreased significantly. Moreover, the magnitude of change in the study group was greater than that in the control group ($P < 0.05$). The total effective rate in the study group was significantly higher as compared to the control group ($P < 0.05$). After treatment, the levels of CD3+ and CD4+ cells in both groups of patients increased significantly, with the study group showing significantly higher levels than the control group, whereas the level of CD8+ cells decreased significantly, with the study group having lower levels than the control group ($P < 0.05$). After treatment, the levels of Tg and CEA in both groups were significantly lowered as compared to before treatment, and the levels of Tg and CEA in the study group were significantly lower than the control group ($P < 0.05$). *Conclusion:* TSH suppression therapy in postoperative thyroid cancer patients can improve thyroid function, suppress the levels of tumor markers, and enhance immune function, thereby achieving good clinical outcomes.

Keywords: TSH suppression therapy; Thyroid cancer; Postoperative; Efficacy; Immune function

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1. Introduction

Thyroid cancer is a relatively common malignant tumor in clinical practice ^[1,2]. It typically grows slowly, but certain types of thyroid cancer can be invasive and have the potential to spread to tissues and organs beyond the thyroid ^[3,4]. If left untreated, tumor progression can pose a risk to the patient's trachea and recurrent laryngeal nerves, and in severe cases, metastasis may occur, leading to a worsened prognosis ^[5]. Treatment options for postoperative thyroid cancer include hormone replacement therapy (HRT) and suppression therapy of thyroid-stimulating hormone (TSH). The main difference between these two treatment methods lies in the range of controlling serum TSH levels. There has been an ongoing debate regarding the advantages and disadvantages of these treatment methods in clinical practice ^[6,7]. Therefore, this study aims to investigate the efficacy and immune function of TSH suppression therapy in postoperative patients with thyroid cancer, aiming to provide insights into the clinical treatment of postoperative thyroid cancer. The findings are reported as follows.

2. Materials and methods

2.1. General information

Sixty patients with thyroid cancer admitted to the Affiliated Traditional Chinese Medicine Hospital of Southwest Medical University from July 2020 to July 2022 were selected as the study subjects. They were randomly assigned using a random number table into a study group and a control group, with 30 patients in each group. In the study group, there were 10 male patients and 20 female patients, with an age range of 25 to 76 years old and an average age of 50.25 ± 9.13 years old. The pathological types included 18 cases of papillary thyroid carcinoma, 5 cases of follicular thyroid carcinoma, 3 cases of medullary thyroid carcinoma, and 4 cases of mixed-type thyroid carcinoma. The tumor stages were as follows: 8 cases in stage I, 14 cases in stage II, and 8 cases in stage III. In the control group, there were 13 male patients and 17 female patients, with an age range of 24 to 78 years old and an average age of 51.25 ± 8.53 years old. The pathological types included 15 cases of papillary thyroid carcinoma, 6 cases of follicular thyroid carcinoma, 4 cases of medullary thyroid carcinoma, and 5 cases of mixed-type thyroid carcinoma. The tumor stages were as follows: 9 cases in stage I, 15 cases in stage II, and 6 cases in stage III. There were no statistically significant differences in general information between the two groups ($P > 0.05$). Both patients and their families were informed about the study protocol and signed informed consent forms approved by the hospital's ethics committee.

2.2. Inclusion and exclusion criteria

Inclusion criteria included patients who meet the requirements for surgical treatment, patients who meet the diagnostic criteria for thyroid cancer and have been confirmed by pathological examination, patients with an estimated survival of more than 12 months, and patients without significant cardiovascular, cerebrovascular, renal, pulmonary, hematological, or mental system diseases, and able to actively participate in the study.

Exclusion criteria included female patients during lactation or pregnancy, patients with significant impairment of vital organs such as the heart, liver, or kidneys, such as congenital heart disease, diabetes, and renal failure, and patients with concomitant other cancers, such as lung cancer.

2.3. Methods

The control group received thyroid HRT. Patients were treated with oral levothyroxine sodium tablets, starting with an initial dose of 50 $\mu\text{g}/\text{day}$, taken in the morning. After two weeks, the dose was increased to 100 $\mu\text{g}/\text{day}$. The study group received TSH suppression therapy, using the same medication and dosage as the control group. During the treatment period, TSH levels were measured monthly for both groups, and the dosage of levothyroxine was adjusted based on the results. In the control group, TSH levels were maintained within the normal range [0.3–5.0 milli-international units per liter (mIU/L)], while in the suppression group, TSH levels were kept within the normal range or slightly elevated but still lower than the range seen in hyperthyroidism (0.05–0.1 mIU/L).

2.4. Observational indicators

Observational indicators in this study included:

- (1) Assessment of thyroid function in both groups of patients: Before and after treatment, 5 mL of fasting venous blood was collected in the morning, and serum was obtained through anticoagulation and centrifugation. TSH, free triiodothyronine (FT3), and free thyroxine (FT4) levels were measured using a fully automated biochemical analyzer, following the instructions provided in the reagent kit. The measurements were performed by two laboratory physicians.
- (2) Comparison of clinical efficacy between the two groups of patients: This includes clinical symptoms

and thyroid function indicators. If clinical symptoms and thyroid function indicators return to normal or improve by more than 30% compared to before treatment, it is considered significantly effective. If both clinical symptoms and thyroid function indicators show improvement by 10% to 30% compared to before treatment, it is considered effective. If there are no significant changes in clinical symptoms and thyroid function indicators, or if the improvement is less than 10% compared to before treatment, it is considered ineffective. The overall effective rate is calculated as (significantly effective/n + effective/n) × 100%.

- (3) Comparison of immune function levels between the two groups of patients: Before and after treatment, 5 mL of fasting venous blood was collected in the morning, and serum was obtained through anticoagulation and centrifugation. Flow cytometry was used to measure the levels of CD3+, CD4+, and CD8+ cells in each group.
- (4) Comparison of tumor marker levels between the two groups of patients: This includes the measurement of thyroglobulin (Tg) and carcinoembryonic antigen (CEA) levels. Before and after treatment, 5 ml of fasting venous blood was collected in the morning, and serum was obtained through anticoagulation and centrifugation. Tg levels were measured using a fully automated electrochemiluminescence immunoassay analyzer, and CEA levels were measured using the same analyzer. All measurements were performed according to the instructions provided in the reagent kit, and two laboratory physicians conducted unified testing to ensure the accuracy of the results.

2.5. Statistical methods

The data were analyzed using SPSS 22.0 software. Continuous variables are presented as mean ± standard deviation (SD). The *t*-test was used to compare continuous variables between the two groups. Categorical variables are presented as [n (%)] and compared using the chi-square test between the two groups. A *P* value of < 0.05 was considered statistically significant for determining differences.

3. Results

3.1. Assessment of thyroid function in the two groups of patients.

Before treatment, there were no significant differences in TSH, FT3, and FT4 levels between the two groups (*P* > 0.05). After treatment, the levels of FT3 and FT4 in both groups of patients increased significantly, while TSH levels decreased significantly. Furthermore, the magnitude of change in the study group was greater than that in the control group (*P* < 0.05). Please refer to **Table 1** for detailed information.

Table 1. Comparison of thyroid function between the two groups of patients (mean ± SD)

Time	Group	Number of cases	TSH (mU/L)	FT3 (pmol/L)	FT4 (pmol/L)
Pre-treatment	Study group	30	4.76 ± 0.82	2.17 ± 0.96	10.85 ± 3.78
	Control group	30	4.52 ± 0.68	2.09 ± 0.71	10.42 ± 3.36
	<i>t</i> value		1.234	0.367	0.466
	<i>P</i> value		0.222	0.715	0.643
Post-treatment	Study group	30	0.97 ± 0.60*	6.25 ± 1.32*	25.04 ± 2.57*
	Control group	30	3.01 ± 0.82#	4.24 ± 1.02#	17.38 ± 2.13#
	<i>t</i> value		10.997	6.600	12.569
	<i>P</i> value		0.000	0.000	0.000

Note: *P* < 0.05 when compared to the pre-treatment values within the same group. * for the study group. # for the control group.

3.2. Comparison of clinical efficacy between the two groups of patients

The overall effective rate of the study group was significantly higher than that of the control group ($P < 0.05$). Please refer to **Table 2** for detailed information.

Table 2. Comparison of clinical efficacy between the two groups of patients [n (%)]

Group	Number of cases	Ineffective	Effective	Significantly effective	Overall response rate
Study group	30	3 (10.00)	13 (43.33)	14 (46.67)	27 (90.00)
Control group	30	10 (33.33)	11 (36.67)	9 (30.00)	20 (66.67)
χ^2 value					4.812
P value					0.028

3.3. Comparison of immune function levels between the two groups of patients

Before treatment, there were no significant differences in the levels of CD3+, CD4+, and CD8+ cells between the two groups of patients ($P > 0.05$). After treatment, the levels of CD3+ and CD4+ cells in both groups of patients increased significantly, with the study group showing significantly higher levels than the control group ($P < 0.05$). Additionally, the level of CD8+ cells decreased significantly, with the study group having lower levels than the control group ($P < 0.05$). Please refer to **Table 3** for detailed information.

Table 3. Comparison of immune function levels between the two groups of patients (mean \pm SD)

Time	Group	Number of cases	CD3+	CD4+	CD8+
Pre-treatment	Study group	30	53.26 \pm 6.31	28.23 \pm 3.12	37.32 \pm 5.16
	Control group	30	53.52 \pm 5.62	28.04 \pm 3.05	37.65 \pm 4.87
	t value		0.169	0.239	0.255
	P value		0.867	0.812	0.800
Post-treatment	Study group	30	67.56 \pm 7.21*	41.32 \pm 4.20*	24.57 \pm 3.22*
	Control group	30	60.03 \pm 6.57 [#]	34.72 \pm 4.36 [#]	30.06 \pm 3.72 [#]
	t value		4.228	5.971	6.112
	P value		0.000	0.000	0.000

Note: $P < 0.05$ when compared to the pre-treatment values within the same group. * for the study group. [#] for the control group.

3.4. Comparison of tumor marker levels between the two groups of patients

There were no significant differences in the levels of Tg and CEA between the two groups of patients before treatment ($P > 0.05$). However, after treatment, the levels of Tg and CEA in both groups were significantly lowered as compared to before treatment, and the levels of Tg and CEA in the study group were significantly lower than the control group ($P < 0.05$). Please refer to **Table 4** for detailed information.

Table 4. Comparison of tumor marker levels between the two groups of patients (mean \pm SD)

Time	Group	Number of cases	Tg (ng/mL)	CEA (U/mL)
Pre-treatment	Study group	30	42.57 \pm 8.56	6.75 \pm 1.52
	Control group	30	43.82 \pm 9.82	6.42 \pm 1.38
	t value		0.526	0.880
	P value		0.601	0.382

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Time	Group	Number of cases	Tg (ng/mL)	CEA (U/mL)
Post-treatment	Study group	30	14.12 ± 3.67*	2.92 ± 0.34*
	Control group	30	19.87 ± 5.06 [#]	3.96 ± 0.57 [#]
	<i>t</i> value		5.038	8.583
	<i>P</i> value		0.000	0.000

Note: $P < 0.05$ when compared to the pre-treatment values within the same group. * for the study group. [#] for the control group.

4. Discussion

Thyroid cancer is a relatively common malignant tumor of the endocrine system, although it accounts for a small proportion of all cancers. However, the incidence rate has been gradually increasing over the years, posing a serious threat to the lives and health of the population [8,9]. Thyroid cancer arises from the uncontrolled proliferation and spread of malignant cells within the thyroid tissue, forming tumors such as papillary carcinoma, follicular carcinoma, medullary carcinoma, and undifferentiated carcinoma [10,11]. Early-stage thyroid cancer usually lacks obvious symptoms, but as the tumor grows and metastasizes, patients may experience symptoms such as neck masses, discomfort in the throat, and hoarseness of voice [12,13]. Compared to some other malignancies, thyroid cancer has a lower degree of malignancy and a slower progression rate. Most thyroid cancer patients achieve good treatment outcomes after surgical removal. However, partial or complete thyroidectomy disrupts the secretion and regulatory stability of thyroid-related hormones in the body, leading to postoperative hypothyroidism. This can significantly impact the body's energy system adjustment, protein metabolism, and stability of endocrine function [14]. Therefore, after thyroid cancer surgery, patients often require endocrine treatment to maintain thyroid hormone levels within a safe range and ensure normal thyroid function [15].

Currently, the endocrine treatment options for post-thyroid cancer surgery patients mainly include HRT and TSH suppression therapy. Most researchers believe that both supplementation and suppression are essential steps because residual thyroid tissue after surgery may grow and recur under the stimulation of TSH [16,17]. Therefore, supplementing levothyroxine can provide normal thyroid hormone levels, while TSH suppression can reduce the stimulation of residual thyroid tissue and decrease the risk of recurrence [18]. However, a small number of researchers believe that the advantages of levothyroxine supplementation outweigh TSH suppression. This is because excessive TSH suppression may lead to side effects, and some studies have shown that TSH suppression does not significantly reduce the recurrence or mortality rate of thyroid cancer [19]. As for the clinical efficacy of the two approaches, there are limited reports available currently, and the results are inconsistent. This may be attributed to the selection of different efficacy endpoints and the influence of other factors [20].

The results of this study showed that after thyroid function treatment, the levels of FT3 and FT4 in both groups of patients significantly increased, while the TSH level significantly decreased, with a greater magnitude of change in the study group compared to the control group ($P < 0.05$). This indicates that TSH suppression therapy can lower TSH levels, increase FT3 and FT4 levels, and reduce thyroid hormone levels. The total effective rate of clinical efficacy in the study group was significantly higher than that in the control group ($P < 0.05$), suggesting that TSH suppression therapy has better clinical efficacy. This is because TSH suppression therapy can increase thyroid hormone levels, and promote protein metabolism and hormone balance.

The results of this study also showed that after TSH suppression therapy, the levels of CD3+ and CD4+ cells in both groups of patients significantly increased, with the study group showing significantly higher levels than the control group, while the level of CD8+ cells significantly decreased, with the study group having lower levels than the control group ($P < 0.05$). This suggests that TSH suppression therapy can

regulate post-thyroid cancer surgery cellular immune function. The development of thyroid cancer is closely related to tumor differentiation and immune function in the body. Thyroid cancer patients have characteristics of immune dysfunction. TSH suppression therapy in post-thyroid cancer surgery can affect tumor differentiation and its relationship with the body's immune function, thereby influencing the characteristics of immune dysfunction in thyroid cancer patients. TSH suppression therapy after thyroid cancer surgery can promote postoperative recovery, reduce the occurrence of tumor recurrence and metastasis, and improve cellular immune function in thyroid cancer patients. Furthermore, the results of this study showed that the levels of tumor markers Tg and CEA after treatment were significantly lower than those in the control group before treatment, and the levels of Tg and CEA in the control group were significantly lower than those before treatment ($P < 0.05$). This indicates that TSH suppression therapy can control the serum levels of Tg and CEA in post-thyroid cancer surgery patients, effectively regulate thyroid hormone levels, stabilize thyroid function, and reduce Tg and CEA levels.

In summary, implementing TSH suppression therapy in post-thyroid cancer surgery patients improves thyroid function, suppresses tumor marker levels of Tg and CEA, and enhances immune function, demonstrating favorable clinical outcomes. These findings are valuable for clinical application and should be promoted.

Disclosure statement

The author declares no conflict of interest.

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