



## Research Article

### Effect of Selenium Yeast Tablets Combined with Levothyroxine Sodium on Thyroid Function and Inflammatory Factors in Patients with Hypothyroidism

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**Received:** September 25, 2019; **Accepted:** May 2, 2024; **Published:** June 6, 2024.

**Cite this paper:** Yuan-Yuan Xing (2024) Effect of selenium yeast tablets combined with levothyroxine sodium on thyroid function and inflammatory factors in patients with hypothyroidism. *Global Journal of Medicine*, 5(1):1-7.

<http://naturescholars.com/gjm.050101>. <https://doi.org/10.46633/gjm.050101>.

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## Abstract

**Objective** To investigate the clinical efficacy of selenium yeast tablets combined with levothyroxine sodium in the treatment of hypothyroidism and its effect on thyroid function and inflammatory factors. **Methods** 110 patients with primary hypothyroidism admitted to The first Affiliated Hospital of Yangtze University from January 2018 to December 2018, and were randomly divided into the observation group (55 cases) and the control group (55 cases). The patients of the control group were given sodium levothyroxine, while the observation group received selenium yeast tablets combined with levothyroxine sodium therapy. The indexes of thyroid function/clinical efficacy/adverse events were compared between the two groups. **Results** The total effective rate of the observation group was 92.73%, and 72.73% in the control group, there was a significant difference between the two groups ( $P<0.05$ ). After treatment,  $T_3$ ,  $T_4$ ,  $FT_3$  and  $FT_4$  levels were significantly increased compared with that before treatment the differences were statistically significant ( $P<0.05$ ). And TSH, TGAb and TPOAb levels were significantly lower compared with that before treatment, and the difference were statistically significant ( $P<0.05$ ). After treatment,  $T_3$ ,  $T_4$ ,  $FT_3$  and  $FT_4$  degree of observation group were better than those of the control group, the differences were statistically significant ( $P<0.05$ ). After treatment, the levels of IL-12 and IFN- $\gamma$  in both groups decreased, but the levels of IL-12 and IFN- $\gamma$  the observation group were lower than those in the control group ( $P<0.05$ ). After treatment, the level of IL-10 increased in two groups, but the level of IL-10 in the observation group was higher than that of the control group ( $P<0.05$ ). There was no significant difference in the incidence of adverse reactions between the two groups ( $P>0.05$ ). **Conclusion** The selenium yeast tablets combined with levothyroxine sodium in treatment of hypothyroidism can obtain obvious therapeutic effects. which can not only improve the levels of various thyroid indexes, but also can improve patient's inflammatory factors levels, with good safety, without serious adverse reactions, therefore, which has important clinical application value.

**Key words:** Selenium; Yeast Tablet; Hypothyroidism; Inflammatory Factor.

## Introduction

Hypothyroidism is a common endocrine disease caused by insufficient synthesis and secretion of thyroid hormones or insufficient physiological effects. According to the pathogenesis, hypothyroidism can be divided into three types: primary hypothyroidism, secondary hypothyroidism and peripheral hypothyroidism, among which primary hypothyroidism is the most common [1,2]. Currently, there is no specific treatment for hypothyroidism in clinic, and drug therapy is the major treatment. Levothyroxine sodium is one of the commonly used drugs, and it can regulate the thyroid-pituitary feedback axis and improve the level of thyroid hormone, but at the same time, long-term medication is required to relieve symptoms[3]. Relevant studies have pointed out that the decrease of thyroid selenium level can cause the destruction of thyroid cells and hypothyroidism [4], therefore, selenium yeast tablets was considered to improve the thyroid function. In this study, the clinical efficacy of selenium yeast tablets combined with levothyroxine sodium in the treatment of hypothyroidism was observed, and its effect on thyroid function and inflammatory factors were reported.

## 1. Data and methods

### 1.1 The general information

110 cases of primary hypothyroidism patients from January 2018 to December 2018 were collected. (1) Inclusion criteria: according to the diagnostic criteria of primary hypothyroidism in 《Guidelines for the Diagnosis and Treatment of Thyroiditis in China》 formulated by the Society of Endocrinology of the Chinese Medical Association[5]; no acute infection occurred within 3 months; (2) Exclusion criteria: complicated malignant tumor; associated with autoimmune diseases; allergy to the constituents of this study; received immune and selenium preparations

tfreatment in recent 3 months; accompanied with serious heart, liver, kidney and other important organ dysfunction; pregnant, parturient and lactating women. According to the random number table method, 110 patients were randomly divided into two groups: 55 in the observation group and 55 in the control group. 14 males and 41 females in the observation group. Age 23~68 years, and the mean age was  $(43.69 \pm 10.38)$  years. The course of disease ranged from 1 to 19 months, with an average of  $(12.35 \pm 3.53)$  months. In the control group, 12 males and 43 females. Age 23~67 years old, and the mean age was  $(41.48 \pm 11.17)$  years. The course of disease ranged from 1 to 17 months, with an average of  $(13.63 \pm 3.81)$  months. There was no statistically significant difference between the two groups in terms of gender, age, disease course and other general information ( $P > 0.05$ ). All patients in this study have been informed consent and signed informed consent, and this study was approved by the medical ethics committee of our hospital.

### 1.2 Treatment Program

The control group was treated with levothyroxine sodium (manufactured by Berlin chemical co, LTD., batch no. 1230101017), with the initial dose of 25-50  $\mu\text{g}/\text{time}$ , once a day, and the dosage was dynamically adjusted according to the patient's symptoms and medication conditions, increasing 25-50  $\mu\text{g}/\text{time}$  every 2-4 weeks, and no more than 200  $\mu\text{g}/\text{time}$ . The treatment regimen of levothyroxine sodium in the observation group was the same as that in the control group. On this basis, selenium yeast tablets (produced by mudanjiang lingtai pharmaceutical co., LTD., Chinese medicine approval word H10940161) were combined with 100-200  $\mu\text{g}/\text{time}$ , once a day. Patients in both groups received continuous treatment for 6 months.

### 2.3 Monitoring Indicators

The clinical efficacy of the two groups was evaluated, and the criteria were as follows :

Markedly effective: clinical symptoms and signs disappeared completely, thyroid index returned to normal;.Effective: the clinical symptoms and signs were significantly improved, and the thyroid index was improved; Invalid: the clinical symptoms, signs and thyroid indicators were not improved[6].

Fasting venous blood of the two groups was collected before and after treatment, centrifuged at a speed of 1500 r/min, and the supernatant was separated 10 minutes later and stored in a refrigerator at  $-70^{\circ}\text{C}$  for testing. Electrochemiluminescence was used to detect the serum triiodothyronine ( $\text{T}_3$ ), thyroxine ( $\text{T}_4$ ), free tetraiodothyronine ( $\text{FT}_4$ ), free triiodothyronine ( $\text{FT}_3$ ), thyroid stimulating hormone (TSH), thyroid peroxidase antibody (TPOAb), thyroglobulin antibody(TGAb), The kit was purchased from Shanghai Enzyme-Linked Biotechnology Co., Ltd; Serum interleukin-10 (IL-10), interleukin-12 (IL-12) and interferon ( $\text{IFN-}\gamma$ ) were detected by elisa. The kit was purchased from Shanghai xinyu biotechnology co., LTD. Adverse reactions were recorded and compared between the two groups.

#### 1.4 Statistical Analysis

SPSS19.0 software was used for statistical analysis. Weighted mean difference(MD) was used for measurement data ( $\bar{x}\pm s$ ) and  $\chi^2$ , while count data were expressed as number (%) and  $P<0.05$  was considered statistically significant.

## 2. Result

### 2.1 Comparison of clinical efficacy between the two groups

The total effective rate of the observation group was 92.73%, and that of the control group was 72.73%. There was a statistical difference in the total effective rate between the two groups ( $P<0.05$ ). As showed in Table 1.

### 2.2 Comparison of thyroid function between the two groups

Before treatment, there were no significant differences in  $\text{T}_3$ ,  $\text{T}_4$ ,  $\text{FT}_3$ ,  $\text{FT}_4$ , TSH, TPOAb and TGAb levels between the two groups ( $P>0.05$ ). After treatment, the levels of  $\text{T}_3$ ,  $\text{T}_4$ ,  $\text{FT}_3$  and  $\text{FT}_4$  in the two groups increased, and the levels of  $\text{T}_3$ ,  $\text{T}_4$ ,  $\text{FT}_3$  and  $\text{FT}_4$  in the observation group were higher than those in the control group, with statistically significant differences ( $P<0.05$ ). After treatment, TSH, TPOAb and TGAb levels in the two group decreased, and TSH, TPOAb and TGAb levels in the observation group were lower than those in the control group, with statistically significant differences ( $P<0.05$ ). As showed in Table 2.

### 2.3 Comparison of inflammatory cytokines between the two groups

Before treatment, there were no statistically significant differences in IL-10, IL-12 and  $\text{IFN-}\gamma$  levels between the two groups ( $P>0.05$ ). After treatment, IL-12 and  $\text{IFN-}\gamma$  levels in both groups decreased, and IL-12 and  $\text{IFN-}\gamma$  levels in the observation group were lower than those in the control group, with statistically significant differences ( $P<0.05$ ). After treatment, the levels of IL-10 increased in both groups, and these were higher than those in the control group, with statistically significant differences ( $P<0.05$ ). As showed in Table 3.

**Table 1 Comparison of clinical efficacy between the two groups**

Group	Cases	Markedly Effective (%)	Effective (%)	Invalid (%)	Total Effective (%)
OG	55	28 (50.91)	23 (41.82)	4 (7.27)	51 (92.73)
CG	55	23 (41.82)	17 (30.91)	15 (27.27)	40 (72.73)
$\chi^2$					7.698
$P$					0.006

**Table 2 comparison of thyroid hormones between the two groups**

Time	Group	T <sub>3</sub> (pmol/L)	T <sub>4</sub> (pmol/L)	FT <sub>3</sub> (pmol/L)	FT <sub>4</sub> (pmol/L)	TSH (mIU/L)	TPOAb (IU/mL)	TGAb (IU/mL)
Prior treatment	OG	0.71±0.10	37.40±6.07	1.73±0.24	4.08±0.29	68.27±8.08	835.43±90.50	501.26±75.74
	CG	0.70±0.12	38.31±6.25	1.75±0.23	4.02±0.28	67.98±8.02	838.04±91.05	501.87±72.55
	<i>t</i>	0.475	0.775	0.446	1.104	0.189	0.151	0.043
	<i>P</i>	0.636	0.440	0.656	0.272	0.851	0.880	0.966
Post treatment	OG	1.90±0.28 <sup>a</sup>	91.64±10.16 <sup>a</sup>	5.60±1.02 <sup>a</sup>	15.67±2.32 <sup>a</sup>	6.73±0.76 <sup>a</sup>	363.08±75.12 <sup>a</sup>	277.05±79.41 <sup>a</sup>
	CG	1.43±0.26 <sup>a</sup>	70.45±9.93 <sup>a</sup>	3.02±1.09 <sup>a</sup>	6.83±0.47 <sup>a</sup>	40.32±6.26 <sup>a</sup>	539.10±10.383 <sup>a</sup>	412.23±83.27 <sup>a</sup>
	<i>t</i>	9.122	11.062	12.317	27.696	39.504	10.136	8.713
	<i>P</i>	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Note: compared with the group before treatment, a: *P* < 0.05.

**Table 3 comparison of inflammatory cytokines between the two groups**

Time	Group	IL-10 (pg/mL)	IL-12 (ng/mL)	IFN-γ (μg/L)
Prior treatment	OG	70.27±18.82	434.01±43.81	5.52±1.23
	<i>t</i>	0.121	0.450	1.221
	<i>P</i>	0.904	0.654	0.225
Post treatment	OG	98.14±22.15 <sup>a</sup>	310.08±30.81 <sup>a</sup>	1.12±0.26 <sup>a</sup>
	CG	89.08±23.06 <sup>a</sup>	321.22±28.02 <sup>a</sup>	1.65±0.20 <sup>a</sup>
	<i>t</i>	2.101	2.016	11.983
	<i>P</i>	0.038	0.046	<0.05

Note: compared with the group before treatment, a: *P* < 0.05

**Table 4 Comparison of adverse reactions between the two groups**

Group	Gastrointestinal discomfort (%)	Weak (%)	Tachycardia (%)	Total number (%)
OG	2 (3.64)	0 (0.00)	1 (1.82)	3 (5.45)
CG	2 (3.64)	1 (1.82)	1 (1.82)	4 (7.27)
<i>x</i> <sup>2</sup>				0.153
<i>P</i>				0.696

**2.4 Comparison of adverse reactions between the two groups**

There were 2 cases of gastrointestinal discomfort and 1 case of tachycardia in the observation group, and the incidence rate of adverse reactions was 5.45%. In the control group, 2 cases of gastrointestinal discomfort, 1 case of fatigue, tachycardia, and the incidence rate was 7.27%, there was no statistically significant difference in the incidence rate of adverse reactions between the two groups ( $P>0.05$ ). (Table 4)

### 3. Discussion

Hypothyroidism is common clinical endocrine disease, the main symptoms include drowsiness, memory loss, mild cognitive impairment, endocrine disorders, anorexia, and muscle weakness, in severe cases, it may slow down the breathing and cause bradycardia or myxedema coma, caused serious harm to patients, so the clinical diagnosis and treatment of hypothyroidism should be highly regarded[1, 7]. However, at present, there is no specific treatment for this disease, and there is a lack of specific radical drugs. Most of them are to maintain thyroid hormone levels and delay or inhibit the progress of the disease. Levothyroxine sodium is an artificial drug with similar efficacy as thyroid tablets. It is converted into triiodothyronine after being absorbed by the human body, which has regulatory effects on the sympathetic adrenal system, lipid metabolism and the feedback axis of the thyroid gland and can improve the level of thyroid hormone[8]. However, levothyroxine sodium requires patients to take medicine for a long time to relief symptom, and the effect is insignificant[3]. Relevant studies have pointed out that decreasing the thyroid selenium level can lead to destruction of thyroid cells and hypothyroidism[4]. Therefore, selenium yeast tablets should be introduced on the basis of levothyroxine sodium to enhance the improvement of thyroid function further more.

Selenium is one of the essential trace elements of human body, which plays an important role in glutathione peroxidation, eliminating free radicals

and maintaining cell membrane integrity. In addition, selenium is mainly distributed in the thyroid gland, it also plays a key role in regulating iodine metabolism and maintaining normal thyroid function[9]. Selenium yeast tablet is an organic combination of selenium element and yeast, and selenium element exists in the form of selenomethionine, which is more conducive to the absorption of selenium element by human body. Selenium yeast tablet is also considered as an effective and safe preparation for selenium supplement[10]. In this study, levothyroxine sodium was used alone in the control group, and levothyroxine sodium combined with selenium yeast tablets were used in the observation group, the results showed that the total effective rate of the observation group was 92.73%, significantly higher than that of the control group ( $P<0.05$ ). The two groups after treatment the  $T_3$ ,  $T_4$ ,  $FT_3$ ,  $FT_4$  levels increased ( $P<0.05$ ), the level of TSH, TPOAb and TGAb was lower ( $P<0.05$ ), but the levels of  $T_3$ ,  $T_4$ ,  $FT_3$ ,  $FT_4$ , TSH, TPOAb, TGAb were superior to control group. Compared with levothyroxine sodium alone, the combination of levothyroxine sodium with selenium yeast tablets more contribute to the improvement of the thyroid function of patients, and this conclusion is consistent with that of Li Haiying et al[11].

IL-10, IL-12 and IFN- $\gamma$  is clinically common inflammatory cytokines. IL-12, IFN- $\gamma$  are mainly secreted by  $Th_1$  cells,  $Th_2$  cells secrete IL-10, the balance of  $Th_1/Th_2$  plays an important role in maintaining normal thyroid function. When  $Th_1$  is dominant, thyroid tissue can be infiltrated by lymphocytes and release large amounts of oxygen free radicals and destroying thyroid cells, further aggravating hypothyroidism[12];  $Th_2$  mediated humoral immunity can stimulate B-cells to produce thyroid excitatory antibodies, promote thyroid hormone synthesis and inhibit hypothyroidism[13]. The results of this study showed that IL-12 and IFN- $\gamma$  levels in both groups decreased after treatment ( $P<0.05$ ), and the IL-12 and IFN- $\gamma$  levels in the observation group were lower than those in

the control group ( $P < 0.05$ ). After treatment, IL-10 level in both groups increased ( $P < 0.05$ ), but IL-10 level in the observation group was higher than that in the control group ( $P < 0.05$ ), suggesting that the combination of levothyroxine sodium and selenium yeast tablets was more conducive to the regulation of Th<sub>1</sub>/Th<sub>2</sub> balance. It is possible that selenium supplementation can increase the levels of Th<sub>2</sub> and decrease Th<sub>1</sub>, thereby increasing IL-10 levels and reducing IL-12 and IFN- $\gamma$  levels[14]. In this study, it was also found that there was no statistical difference in the incidence of adverse reactions between the two groups ( $P > 0.05$ ), indicating that the combination of selenium yeast tablets did not increase the toxic and side effects, and it was safe and reliable.

In conclusion, selenium yeast tablets can increase IL-10 and decrease IL-12 and IFN- $\gamma$ , and regulate the balance of Th<sub>1</sub>/Th<sub>2</sub>, so it would help to improve the thyroid function of patients with hypothyroidism. In addition, it is safe and reliable, and worthy of clinical reference

## Declarations

### 1) *Consent to publication*

We declare that all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement, and followed publication ethics.

### 2) *Ethical approval and consent to participants*

We declare that our research protocol involving humans were approved by our Institutional Ethics Committee and we obtained Informed Consent from Participants enrolled in this study.

### 3) *Disclosure of conflict of interests*

We declare that no conflict of interest exists.

### 4) *Funding*

None

### 5) *Availability of data and material*

We declare that the data supporting the results reported in the article are available in the published article.

### 6) *Author Contributions*

Authors contributed to this paper with the design (YYX), literature search (YYX), drafting (YYX), revision (YYX), editing (YYX) and final approval (YYX).

### 7) *Acknowledgement*

None

### 8) *Author biography*

None

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