

Analysis of Effectiveness, Thyroid Function and Prognosis of Levothyroxin Sodium and Selenium Yeast Tablets for Differentiated Thyroid Carcinoma

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Wang *et al.*: Levothyroxin Sodium and Selenium Yeast Tablets for Thyroid Carcinoma

This paper mainly analyzes the influence of levothyroxin sodium tablets plus selenious yeast tablets on the effectiveness, thyroid function and prognosis of post-surgical individuals with differentiated thyroid carcinoma. This study selected 190 post-surgical differentiated thyroid carcinoma individuals treated between January 2021 and June 2022. 90 individuals were included in the control group who received levothyroxin sodium tablets therapy and 100 individuals in the research group receiving levothyroxin sodium tablets with selenious yeast tablets therapy. The effectiveness, safety symptoms such as headache, palpitations, insomnia, and gastrointestinal discomfort was assessed. Thyroid function such as thyroid-stimulating hormone, serum free triiodothyronine and free thyroxine between the two groups were evaluated. Further, the prognosis which included recurrence and disease-free survival during 1 y follow-up was observed. Then, differentiated thyroid carcinoma-related markers such as anti-thyroid peroxidase antibody, thyroglobulin and anti-thyroglobulin antibody were comparatively analyzed. The evaluation results showed a markedly higher total effective rate and an evidently lower adverse drug reaction rate in the research group compared with the control group. Besides, thyroid-stimulating hormone, anti-thyroid peroxidase antibody, thyroglobulin and anti-thyroglobulin antibody of the research group reduced notably after medication, lower versus the control group, while free triiodothyronine and free thyroxine elevated statistically, higher compared with the control group. Conclusively, the use of levothyroxin sodium tablets along with selenious yeast tablets for post-surgical differentiated thyroid carcinoma can significantly enhance effectiveness, thyroid function and prognosis necessitating clinical popularization.

Key words: Thyroid carcinoma, levothyroxin, thyroid-stimulating hormone, thyroxine, thyroglobulin antibody, thyroid peroxidase antibody

Thyroid Cancer (TC) is an endocrine malignancy, characterized by Differentiated Thyroid Carcinoma (DTC), which accounts for over 90 % of all TC cases^[1,2]. DTC includes papillary and follicular thyroid carcinoma^[3]. According to DTC statistics, DTC tends to occur in women, with a 4-fold risk in women than in men^[4]. Surgery is the mainstay of treatment for DTC, mostly with total thyroidectomy or lobectomy^[5], contributing to a 10 y cause-specific survival rate as high as 99 % in individuals undergoing either of the two surgical procedures^[6]. However, despite the iterative improvement in DTC diagnosis and treatment over the past few decades, 5 %-10 % of DTC patients are still threatened with death and are associated with a high risk of recurrence^[7].

Therefore, adjuvant means are needed to improve the efficacy and prognosis of post-surgical DTC patients. Levothyroxin Sodium Tablets (LST) are essentially levorotatory isomers of thyroxine that can be used as alternative therapy for patients with hypothyroidism^[8,9]. LST has been reported to improve pregnancy outcomes in patients with subclinical hypothyroidism and promote neuro-intellectual development in offspring^[10]. It also benefits the postoperative recovery and Thyroid Function (TF) repair of DTC patients; however, patients may demonstrate incomplete adherence to treatment and under- or overdosing may lead to hypothyroidism or hyperthyroidism^[11-13]. Selenium homeostasis is

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known to play a key role in the regulation of TF. In the absence of selenium, the synthesis of thyroid hormones in the body will be inhibited, which will stimulate the hypothalamus-pituitary axis to secrete excessive Thyroid-Stimulating Hormone (TSH), leading to hydrogen peroxide accumulation in thyroid tissue, inducing thyroid cell damage and fibrosis development^[14-16]. Selenious Yeast Tablets (SYT), an organic form of selenium supplement that have also been shown to exert protective effects on the salivary glands of DTC patients^[17].

Given the lack of reports on the potential clinical advantages of LST combined with SYT in post-surgical DTC patients, this study will validate to contribute to the improvement of efficacy and prognosis in DTC patients after surgery.

MATERIALS AND METHODS

General data:

In this study, 190 post-surgical DTC patients who received treatment at our hospital admitted from January 2021 to June 2022 were strictly screened out based on the eligibility criteria and were assigned into two groups, control and research groups. Control group (n=90) was given LST while the research group (n=100) was given LST combined with SYT. No notable inter-group difference was identified in baseline data ($p>0.05$), suggesting clinical comparability. The hospital's ethics committee approved the study.

Inclusion criteria: All patients who received total or subtotal thyroidectomy and were confirmed as DTC without distant metastasis or residual recurrence by imaging examination and histopathology; patients with symptoms such as chills, fatigue and memory loss; patients who are willing to complete 1 y follow-up; patients having intact and complete patient records with no contraindications to treatment were included in this study.

Exclusion criteria: Pregnant or lactating women; patients with severe cardiac, pulmonary, or hepatorenal dysfunction; patients with coagulation dysfunction, autoimmune system defects and other malignancies and patients having the inability to communicate normally due to mental disorders or cognitive impairment were excluded from this study.

Treatment method:

Control group received 50 $\mu\text{g}/\text{time}$ of LST, once/d. After 3 w of treatment, the dose was increased to 100 $\mu\text{g}/\text{time}$ which was continued for another 3 w. On

this basis, the research group was additionally given 200 $\mu\text{g}/\text{time}$ of SYT, once/d for 6 w.

Observation indicators:

Clinical efficacy: The clinical efficacy was evaluated according to the effectiveness grades which included marked effectiveness, effectiveness and ineffectiveness. Here, marked effectiveness refers to relieved clinical symptoms and signs. Additionally marked effectiveness also denotes the return of TF indices such as serum TSH, Free Triiodothyronine (FT3) and FT4 to normal levels. Effectiveness means certain alleviation of clinical symptoms and signs; return of FT3 and FT4 to normal levels, and the decrease of TSH level. While, ineffectiveness corresponds to none or slight relief of clinical symptoms and signs. Further, it also shows no obvious increase in serum FT3 and FT4 levels, and the increase of TSH level. The total effective rate is denoted by the sum of the number of effective cases (n) and the number of effective patients as a percentage of the total number of cases.

Safety: The medication safety was evaluated by observing and recording the number of adverse events between the research and control groups such as headache, palpitations, insomnia and gastrointestinal discomfort.

TF: Before and after treatment, 5 ml of venous blood from each patient was collected. The supernatant was separated by centrifuging the serum using radioimmunoassay technique of TF indices such as TSH, FT3 and FT4.

Prognosis: After discharge, all the patients received 1 y outpatient follow-up by different means of communication such as telephone, Quick Question (QQ), Wechat and email, and other means once for every 3 mo. The recurrence rate and disease-free survival rate of both the groups were statistically compared.

DTC-related markers: Electrochemiluminescence immunoassay was performed to determine the serum levels of anti-Thyroid Peroxidase Antibody (TPOAb), Thyroglobulin (Tg) and anti-Thyroglobulin Antibody (TGAb) before and after treatment.

Statistical methods:

This study employed Statistical Package of Social Sciences (SPSS) version 20.0 for statistical analysis and $p<0.05$ as the significance threshold. Categorical variables (e.g., gender and clinical staging) and continuous variables were statistically described

as number of cases/percentage (n/%) and Standard Deviation (SD)±Statistical Error of Mean (SEM), respectively. Among them, categorical variables were analyzed by the Chi-square (χ^2) test, while continuous variables were tested by the independent samples t test and paired t test for the identification of inter- and intra-group differences, respectively.

RESULTS AND DISCUSSION

Baseline data analysis of all the DTC patients in the two groups were compared analysed. We determined no statistical inter-group difference in gender, age, disease course, Body Mass Index (BMI) and other baseline data ($p>0.05$) (Table 1).

Further, the impact of combined effect of LST and SYT on efficacy in post-surgical DTC patients of the two groups. The total effective rate of the control group was 83.33 %, which was notably reduced compared with research group (93.00 %), with a statistical inter-group difference ($p<0.05$) (Table 2).

Similarly, the combined effect of LST and SYT on medication safety in post-surgical DTC patients of both the groups was studied. Statistics on the incidence of headache, palpitations, insomnia and gastrointestinal discomfort in post-surgical DTC patients revealed an adverse drug reaction rate of

8.00 % in research group, lower than the 17.78 % in the control group ($p<0.05$) (Table 3).

Subsequently, the influence of combined effect of LST and SYT on TF of DTC patients of the two groups were assessed. Similar levels of TF indices such as TSH, FT3 and FT4 were found in the two groups before medication ($p>0.05$). After medication, TSH in both groups was inhibited, while FT3 and FT4 were increased ($p<0.05$). Moreover, research group exhibited lower TSH and higher FT3 and FT4 levels than the control group ($p<0.05$) (fig. 1).

Prognosis after the administration of LST and SYT among DTC patients in the two groups was observed. Both the groups completed 1 y follow-up. The data revealed a lower recurrence rate and a higher disease-free survival rate in research group vs. control group ($p<0.05$) (Table 4).

Further, the influence of LST and SYT on DTC-related markers among all the DTC patients was observed. Detection of the DTC-related markers such as TPOAb, Tg and TGAb in the two groups revealed no marked inter-group difference before medication ($p>0.05$). All these indices reduced statistically in both groups after medication, with even lower levels in research group ($p<0.05$) (fig. 2).

TABLE 1: BASELINE DATA ANALYSIS OF POST-SURGICAL DTC PATIENTS

Indicators	Control group (n=90)	Research group (n=100)	χ^2/t	P
Gender (male/female)	25/65	40/60	3.144	0.076
Age (y)	38.43±8.81	37.38±12.97	0.646	0.519
Disease course (y)	2.09±0.88	2.23±0.92	1.069	0.286
BMI (kg/m ²)	23.19±2.73	23.12±3.76	0.145	0.885
Clinical staging (I/II/III)	60/25/5	65/22/13	3.430	0.180
Lesion diameter (cm)	1.79±0.32	1.69±0.43	1.802	0.073

TABLE 2: IMPACT OF LEVOTHYROXIN SODIUM and SELENIOUS YEAST TABLETS ON THE EFFICACY IN POST-SURGICAL DTC PATIENTS

Indicators	Control group (n=90)	Research group (n=100)	χ^2/t	p
Marked effectiveness	35 (38.89)	57 (57.00)		
Effectiveness	40 (44.44)	36 (36.00)		
Ineffectiveness	15 (16.67)	7 (7.00)		
Total efficacy=Marked effectiveness+effectiveness	75 (83.33)	93 (93.00)	4.323	0.038

TABLE 3: EFFECT OF LEVOTHYROXIN SODIUM AND SELENIOS YEAH TABLETS ON MEDICATION SAFETY IN POST-SURGICAL DTC PATIENTS

Indicators	Control group (n=90)	Research group (n=100)	χ^2	p
Headache	3 (3.33)	3 (3.00)		
Palpitations	1 (1.11)	0 (0.00)		
Insomnia	7 (7.78)	2 (2.00)		
Gastrointestinal discomfort	5 (5.56)	3 (3.00)		
Total	16 (17.78)	8 (8.00)	4.104	0.043

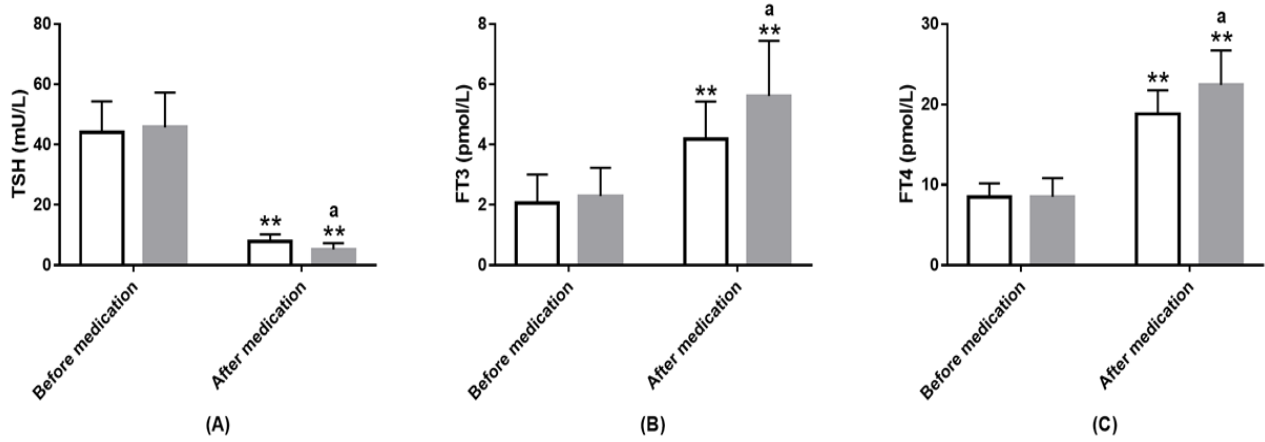


Fig. 1: Pre- and post-treatment levels and influence of levothyroxin sodium and selenious yeast tablets on thyroid function of post-surgical DTC patients in two groups, (A): TSH; (B): FT3 and (C): FT4

Note: **p<0.05 vs. before medication and ^ap<0.05 vs. control group, (□): Control and (■): Research group

TABLE 4: IMPACT OF LEVOTHYROXIN SODIUM AND SELENIOS YEAH TABLETS ON THE PROGNOSIS OF POST-SURGICAL DTC PATIENTS

Indicators	Control group (n=90)	Research group (n=100)	χ^2	p
Recurrence	8 (8.89)	0 (0.00)	9.280	0.002
Disease-free survival	82 (91.11)	100 (100.00)	9.280	0.002

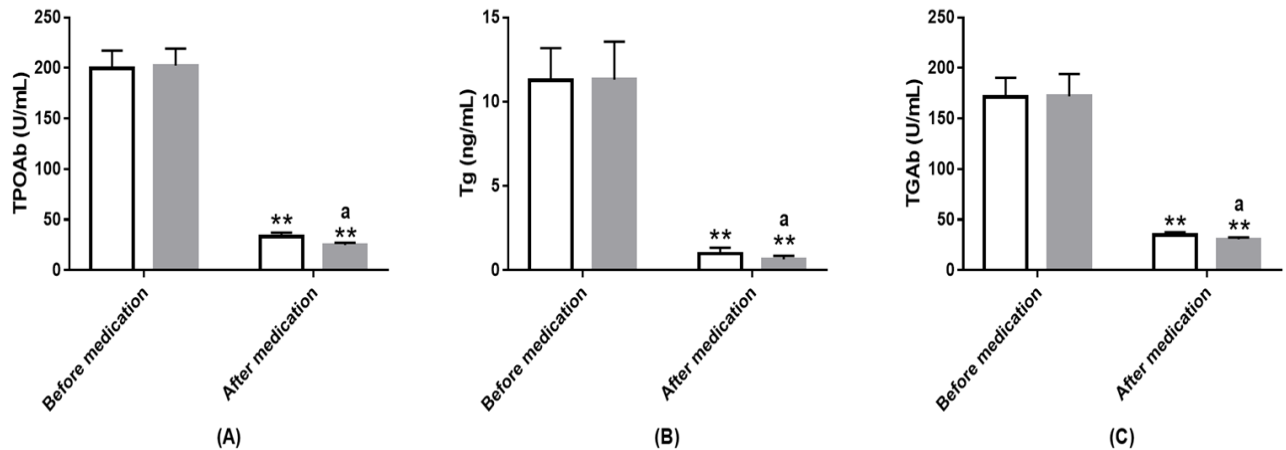


Fig. 2: Pre- and post-treatment levels of DTC-related markers influence on levothyroxin sodium tablets and selenious yeast tablets in patients of two groups, (A): TPOAb; (B): Tg and (C): TGAb

Note: **p<0.05 vs. before medication and ^ap<0.05 vs. control group, (□): Control and (■): Research

This study included 190 post-surgical DTC patients to comprehensively analyze the clinical application value of LST and SYT in such patients from the perspectives of effectiveness, safety, TF, prognosis and DTC-related markers, confirming that the combination of LST and SYT has significant clinical advantages for post-surgical DTC patients. We hereby report in detail.

We first identified a higher total effective rate in research group vs. control group which was found to be 93.00 % vs. 83.33 % respectively, indicating that LST with SYT used in post-surgical DTC patients is effective in significantly improving therapeutic effectiveness. The major effective component of SLT is levothyroxine sodium, which can be used for the treatment of non-toxic goiter and hyperthyroidism in addition to suppressive therapy following thyroidectomy^[18-20]. Levothyroxine present in it can replace thyroxine, which is converted into T3 in peripheral organs and binds to corresponding receptors to play a therapeutic role^[21].

As shown by basic experiments, selenium supplements inhibit TC cell proliferation by up-regulating the expression of Growth Arrest and Deoxyribonucleic Acid (DNA) Damage-inducible (GADD) gene 153/34^[22]. Other evidence has reported the significant negative correlation between serum selenium concentration and disease staging in TC patients, suggesting that high selenium concentration is helpful to inhibit TC procession^[23]. According to the safety analysis, the incidence of adverse drug reactions such as headache, palpitations, insomnia and gastrointestinal discomfort was significantly lower in research group than in the control group which was found to be 8.00 % vs. 17.78 %, similar to the research results of Rosário *et al.*^[24].

TSH, FT3 and FT4 are all auxiliary diagnostic and therapeutic indicators to guide thyroid dysfunction, among which TSH level is significantly and positively correlated with the risk of DTC. FT3 has a certain correlation with the symptom relief of DTC patients and FT4 can help to predict the risk of potential liver dysfunction in male DTC patients after drug treatment to a certain extent^[25-27]. In the subsequent analysis of TF, research group showed markedly reduced TSH and elevated FT3 and FT4 after medication, with lower TSH, and higher FT3 and FT4 than control group, suggesting that LST and SYT can significantly improve TF in post-surgical DTC patients. This may be related to the antioxidant defense effect of some selenoproteins provided

by SYT in thyroid glands by removing oxygen free radicals associated with thyroid hormone production^[28]. After 1 y of follow-up, the recurrence rate was found to be markedly lower in research group than the control group which was found to be 0.00 % vs. 8.89 %, while the disease-free survival rate was significantly higher (100.00 % vs. 91.11 %), suggesting that LST and SYT has significant advantages in improving the prognosis of post-surgical DTC patients. It is conducive to reducing the risk of recurrence and improving the disease-free survival rate. When analyzing DTC-related markers, we found that the levels of TPOAb, Tg and TGAb in research group were evidently lower than the baseline values and those of CG, demonstrating that LST with SYT can effectively alleviate disease progression by downregulating TPOAb, Tg and TGAb in post-surgical DTC patients. In the study of Pang *et al.*^[29], the application of LST plus iodine-131 in patients undergoing thyroidectomy not only helps to improve the removal rate of residual thyroid tissue and curative efficacy, but also lowers the risk of recurrence and effectively reduces the serum Tg level, similar to our findings.

To sum up, LST plus SYT for post-surgical DTC patients is conducive to reducing the risk of adverse drug reactions, improving TF and prognosis, and significantly lowering the levels of TPOAb, Tg and TGAb to alleviate disease progression.

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Conflict of interests:

The authors declared no conflict of interests.

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