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Research Article

Effect of Integrated Treatment with Traditional Chinese Medicine on Hashimoto's Thyroiditis Patients

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What is Known and Objective. To explore the effects of traditional Chinese medicine (TCM) combined with levothyroxine (L-T4) on thyroid autoantibodies, inflammation, and sleep quality in Hashimoto's thyroiditis patients. *Methods*. Patients were randomly divided into group A and group B. Group A was treated with L-T4 alone, while group B was treated with integrated TCM and L-T4. TCM symptoms were quantified before and after treatment as well as PSQI. Blood samples were taken to detect clinical indicators and thyroid autoantibodies. Cytokines in serum and thyroid tissues were analyzed by ELISA and RT-PCR. *Results and Discussion*. Totally, 196 patients were enrolled in the study, and there were no differences between group A and group B at the baseline. TCM treatment effectively reduced the levels of TGAb and TPOAb and was a protective factor for the improvement of Hashimoto's thyroiditis antibody titers, $p < 0.05$. The serum expressions of IL-17A, IL-6, and IFN-γ in group B after treatment were lower than those in group A and before, while the IL-10 level was raised from the baseline, $p < 0.05$. Similar results were found in the comparison of IL-17A, IFN-γ, and IL-10 in thyroid tissues of group A, B, and control, $p < 0.05$. Besides, with integrated treatment, all TCM symptoms except for poor memory were improved as well as sleep quality and mood, $p < 0.05$. However, these changes were not observed before and after treatment with L-T4 in group A. *What is New and Conclusion*. The integrated treatment with TCM had a significant effect on thyroid autoantibodies, inflammation, and sleep quality in Hashimoto's thyroiditis patients and provided a new and effective method for future treatment.

1. What Is Known and Objective

Hashimoto's thyroiditis (HT), also known as chronic lymphocytic thyroiditis (CLT), is a common clinical autoimmune thyroid disease (AITD) [1]. In recent years, the incidence of HT has increased. The latest flow survey data show that [2, 3] at present, the prevalence of HT has increased to 5–10%, and the course of disease is prolonged, which is common in women. The immune mechanism of the disease is complex. The increase of serum TGAb and TPOAb is its clinical marker, which often coexists with other autoimmune diseases and tumor diseases, and the harm to health cannot be ignored. At present, L-T4 is the main drug used in western medicine to treat HT. L-T4 can increase the level of thyroxine in patients with clinical hypothyroidism and subclinical hypothyroidism and reduce TSH. The curative effect is positive, but it is easy to cause insomnia, palpitation, spontaneous sweating, and even myocardial ischemia. Long-term use has the risk of osteoporosis and fracture.

Chinese herbal medicine, as traditional Chinese medicine, has unique advantages in those aspects of medical treatment, prophylaxis, and health protection and has been paid more and more attention and acceptance from researchers at home and abroad. HT belongs to the category of "gall disease" in traditional Chinese medicine. It is caused by internal emotional injury, diet and water, and soil loss, resulting in circulation of vital energy stagnation, phlegm coagulation, and blood stasis in front of the neck. The inflammatory process in the early stage of the disease is consistent with the theory of "excess circulation is fire" in TCM [4]. The pharynx where the thyroid located is the part

of the liver meridian, so "gall disease" is closely related to the liver. The traditional Chinese medicine "Shu Gan Qing Huo Decoction" is cold in nature and belongs to the liver meridian. It has the functions of clearing heat and detoxification, cooling blood and eliminating spots, and purging fire and calming shock. Previous study used "Shu Gan Qing Huo Decoction" to treat HT in the early stage and found that it may relieve symptoms and reduce thyroid autoantibodies [5].

Currently, there is no specific treatment for HT, and oral medication, selenium, and L-T4 tablets, as well as surgery and low-intensity laser methods, are not confirmed clear therapeutic effects, or the long-term toxicity and side effects are unpredictable. Therefore, this topic organically combines the above two methods by the randomized controlled study, scientifically summarizes their respective advantages, evaluates the efficacy of integrated treatment with TCM, and explores a new scheme for HT intervention.

2. Methods

2.1. Patients. Hashimoto's thyroiditis patients were collected from the outpatient department of Endocrinology, Huadong Hospital Affiliated to Fudan University, Shanghai, China, during January 2019 to December 2021. They were divided randomly into two groups by a random number table: group A was treated with L-T4 alone, while group B was combined with Chinese herbal medicine after 2-week L-T4 treatment. The estimated sample size was about 200, based on the calculated formula: $n = z^2\sigma^2/d^2$ and the pre-experiment. Total treatment course of the two groups was 12 weeks, and the primary outcomes were thyroid function and cytokines before and after treatment. The secondary outcomes were TCM symptoms, PSQI, and HAMA scores. The calculation formula for BMI was weight divided by the square of height ($\text{BMI} = \text{kg/m}^2$). The clinical study was approved by the Ethics Committee of Huadong Hospital affiliated to Fudan University (Number: 20190108), and all subjects were registered anonymously.

2.2. Diagnostic Criteria. The diagnostic criteria of HT in all patients were referred to Chinese guidelines for the diagnosis and treatment of thyroid diseases issued by the endocrinology branch of the Chinese Medical Association [6]. The details were as follows: (1) goiter, tough texture, isthmic pyramidal lobe enlargement or asymmetry, or accompanied by nodules; (2) serum TPOAb and or TGAb were positive; (3) thyroid ultrasound examination showed that the thyroid gland showed diffuse uneven changes, or with isthmus thickening, uneven hypoechoic areas of varying degrees, or with thyroid nodules; (4) thyroid fine-needle biopsy revealed diffuse lymphocyte and plasma cell infiltration, lymphoid follicles, and fibrous tissue hyperplasia in the thyroid gland. HT can be diagnosed if both (1) (2) (3) and /or (4) were present.

Hypothyroidism was a systemic metabolic syndrome caused by decreased synthesis and secretion of thyroid hormone or weakened action of peripheral tissues. According to the degrees of hypothyroidism, it can be divided into clinical hypothyroidism and subclinical hypothyroidism. Clinical hypothyroidism: the laboratory examinations showed an increase in serum TSH and a decrease in FT4 or TT4. Subclinical hypothyroidism: there may be no obvious hypothyroidism in clinical performance, but laboratory tests showed elevated TSH and normal FT4 or TT4.

2.3. Inclusion and Exclusion Criteria. Inclusion criteria were (1) patients complied with the HT diagnostic standard; (2) combined with hypothyroidism or subclinical hypothyroidism; (3) the age ranged from 18 to 80 years; (4) willing to be treated with Chinese herbal medicine; (5) those who had signed on the written informed consent for participating in the trial.

Exclusion criteria were (1) patients with infiltrative exophthalmos and other thyroid diseases; (2) have serious heart, liver, kidney complications, and serious diseases such as cancer; (3) pregnant and lactating women; (4) allergic to traditional Chinese medicine or allergic constitution; (5) mental illness and unable to cooperate; (6) those who were currently participating in other clinical research.

2.4. Treatment. Levothyroxine (L-T4) preparation: the L-T4 tablets were produced by the German Merck company, with 50 μg per tablet, taken in the morning, once a day. The thyroid levels were remeasured after 6 and 12 weeks of treatment, and individualized L-T4 doses were formulated according to the thyroid function to ensure that there was no overdose. The prescription of traditional Chinese medicine "Shu Gan Qing Huo recipe": bupleurum root 6 g, white peony root 6 g, jiaobaizhu 9 g, white Poria cocos 9 g, Ligusticum chuanxiong 6 g, tangerine peel 6 g, Prunella vulgaris 9 g, Scutellaria baicalensis 9 g, and indigo naturalis 3 g. The granules were packed in two bags according to the daily dose, one bag each time, twice a day, and decocted with warm water half an hour after breakfast and dinner.

2.5. Clinical Observations

2.5.1. Symptoms. The main TCM symptoms of Hashimoto's thyroiditis patients, including weakness, irritability, poor appetite, neck discomfort, and poor memory, were divided into 4 grades according to different degrees of symptoms. None marked as 0, mild as 1, moderate as 2, and severe as 3 points.

2.5.2. Sleep Quality. The Pittsburgh sleep quality index (PSQI) is a self-reported questionnaire used to evaluate sleep quality and disorders. It consists of seven components [7], the score range of each question is 0–3, and the total score is 0–21. The higher the score, the worse the sleep quality.

2.5.3. Anxiety. The Hamilton anxiety scale (HAMA) was used to assess the severity of patients' anxiety symptoms. All options were scored 0–4 points with a total of 14 items. Level

0 was asymptomatic, and level 4 was extremely severe. All participants had 15 minutes to complete the questionnaire under the guidance of a trained researcher.

2.6. Laboratory Determination. All participants were instructed to maintain their recommended dietary, medication, and exercise programs. 10 ml of fasting venous blood was collected after fasting for 8–12 hours. Fasting blood glucose (FPG) (glucose oxidase method) and glycosylated hemoglobin (HbA1c) (affinity chromatography colorimetry) were determined. Liver function (ALT), renal function (Cr), eGFR, total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), and thyroid function (radioimmunoassay) were measured by using the Cobas 8000 automatic biochemical immune analyzer. Serum cytokines, including interleukin (IL)-17A, IL-6, IL-10, and interferon-γ (IFN-γ), were detected by ELISA (R&D, Minneapolis, Minnesota; RayBiotech, Peachtree Corners, Georgia; Invitrogen, Carlsbad, California) according to the manufacturer's instructions [8].

2.7. Real-Time qPCR. The total RNA was isolated from thyroid fine-needle aspiration biopsy samples with Trizol reagent (Invitrogen Life Technologies Inc., Carlsbad, CA, USA), and GAPDH was used as the internal control. A quantity of 1 μg RNA was reverse-transcribed using the MMLV reverse transcription system (Promega, Madison, WI, USA) as previously described [9]. Real-time reverse transcription-polymerase chain reactions (RT-PCR) were performed using TB Green Premix Ex Taq (RR420A; Takara) through the StepOne Real-Time PCR System (Applied Biosystems, Foster City, California). Relative expression of mRNA was calculated after normalization to GAPDH, using the comparative $2^{-\Delta\Delta Ct}$ method as described previously [10].

2.8. Statistical Analysis. All results were expressed as means ± standard deviations. Analysis of comparisons between the groups was performed by Student's *T*-test or one-way ANOVA after normality assessment. For normally distributed variables, the unpaired Student's *t*-test was used for comparisons between the two groups and the paired Student's *t*-test to assess differences before and after treatment. Categorical variables were analyzed by using the chi-squared test. Logistic regression statistical analyses were carried out using SPSS 23.0 software for Mac. A level of probability up at $p < 0.05$ was set up as statistically significant.

3. Results

3.1. Clinical Characteristics. The flow diagram of this study is shown in Figure 1. A total of 263 subjects were enrolled in our study, of which 52 were excluded according to in- and ex-criteria and 15 were dropped out of the trial; most of them were caused by bad compliance. Finally, there were 102 in group A (17 males and 85 females) and 94 in group B (15 males and 79 females), with an average age of

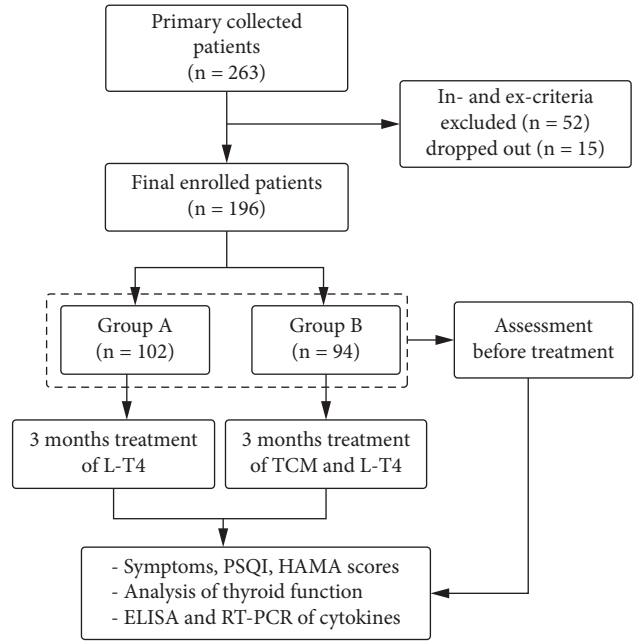

Figure 1: The flow diagram of the study.

53.60 ± 16.64 years and 49.81 ± 13.60 years, respectively, $p > 0.05$. At the baseline, there was no significant difference between the two groups in BMI, FPG, HbA1c, ALT, Cr, TC, TG, LDL-C, and HDL-C, $p > 0.05$. Thus, the influence of confounding factors was excluded in the subsequent statistical results. The clinical characteristics of the participants are summarized in Table 1. The average daily dose of L-T4 was 30.0 μg in group A and 28.12 μg in group B at the terminal point, $p > 0.05$.

3.2. Symptoms' Assessment. The curative effect standard is drafted with reference to the guiding principles for clinical research of new Chinese medicine (Trial) [11]. Clinical recovery: the clinical symptoms and signs of TCM disappear or basically disappear, and the score reduction rate is ≥90%. Significant effect: the clinical symptoms and signs of TCM were significantly improved, and the score reduction rate was ≥70% and <90%. Effective: the clinical symptoms and signs of TCM are improved, and the score reduction rate is ≥30% and <70%. Ineffective: the clinical symptoms and signs of TCM have not improved significantly, or even worsened, and the score reduction rate is less than 30%.

Before treatment, the quantifications of all symptoms in group A and group B were not statistically significant. After treatment with integrated TCM and L-T4, all symptoms were improved except for poor memory, $p < 0.05$. See Table 2 for details. The effective rates of group B in treating TCM syndromes of "irritability," "poor appetite," and "neck discomfort" were 37.5%, 38.7%, and 56.3%, respectively, significantly higher than those of group A, 5%, 10%, and 20%, $p < 0.05$. The total effective rate of clinical efficacy was 78.43% (80/102) in group B and 55.32% (52/94) in group A. Therefore, the TCM treatment group was superior to the control group ($p < 0.05$).

Table 1: Clinical characteristics of participants between two groups.

Variables	Group A	Group B	P
Number (M/F)	102 (17/85)	94 (15/79)	0.346
Age (years)	53.60 ± 16.64	49.81 ± 13.60	0.292
BMI (kg/m^2)	23.34 ± 3.23	24.69 ± 3.64	0.847
Duration (years)	5.41 ± 3.95	6.80 ± 2.2	0.270
FPG (mmol/L)	5.32 ± 1.41	5.65 ± 1.93	0.063
HbA_1C (%)	5.58 ± 0.77	5.71 ± 0.63	0.283
ALT (U/L)	22.3 ± 14.9	21.8 ± 15.7	0.717
Cr (μmol/L)	74.45 ± 9.36	78.23 ± 10.55	0.322
eGFR (ml/min)	79.10 ± 32.74	86.3 ± 29.29	0.506
Cholesterol (mmol/L)	4.77 ± 1.25	4.49 ± 2.28	0.433
Triglyceride (mmol/L)	1.63 ± 1.32	1.57 ± 1.08	0.122
LDL-C (mmol/L)	2.45 ± 0.94	3.06 ± 1.34	0.752
HDL-C (mmol/L)	1.41 ± 0.39	1.38 ± 0.55	0.493

Table 2: Comparison of symptom quantifications before and after treatment.

Symptoms	Quantifications	Before		P	After		P
		Group A	Group B		Group A	Group B	
Weakness				0.432			<0.001
n (%)	0	0 (0.0)	0 (0.0)		3 (2.5)	9 (9.4)	
	1	33 (32.5)	21 (21.9)		51 (50.0)	79 (84.4)	
	2	64 (62.5)	70 (75.0)		48 (47.5)	6 (6.3)	
	3	5 (5.0)	3 (3.1)		0 (0.0)	0 (0.0)	
Irritability				0.600			0.016
n (%)	0	0 (0.0)	0 (0.0)		0 (0.0)	9 (9.4)	
	1	51 (50.0)	41 (43.8)		56 (55.0)	65 (68.8)	
	2	51 (50.0)	53 (56.3)		46 (45.0)	20 (21.9)	
Poor appetite				0.938			0.004
n (%)	0	0 (0.0)	0 (0.0)		0 (0.0)	15 (15.6)	
	1	56 (55.0)	53 (56.4)		61 (60.0)	64 (68.8)	
	2	43 (42.5)	38 (40.6)		41 (40.0)	15 (15.6)	
	3	3 (2.5)	3 (3.1)		0 (0.0)	0 (0.0)	
Neck discomfort				0.548			0.011
n (%)	1	23 (22.5)	12 (12.5)		31 (30.0)	56 (59.4)	
	2	56 (55.0)	62 (65.6)		61 (60.0)	35 (37.5)	
	3	23 (22.5)	20 (21.9)		10 (10.0)	3 (3.1)	
Poor memory				0.711			0.785
n (%)	1	46 (45.0)	38 (40.6)		64 (62.5)	62 (65.6)	
	2	56 (55.0)	56 (59.4)		38 (37.5)	32 (34.4)	

3.3. Thyroid Function and Antibodies. With traditional Chinese medicine and L-T4, the average value of FT4 in both groups was increased and TSH decreased when compared with before treatment, $p < 0.05$ (Figure 2(a)). That is, the hypothyroidism of patients in the two groups could be recovery after treatment. In addition, the paired t test showed that after treatment the thyroid autoantibodies in group B were far less than before, though no statistical difference in value except for TPOAb (Figure 2(b)). However, the proportion of patients with one improved thyroid antibody titer in group A was 52.5%, while that in group B was 84.4%, $p = 0.006$. The proportion of both thyroid antibody tilters improved was 15.0% in group A and 53.1% in group B, $p = 0.001$. Of note, the improvement of antibody titers referred to a decrease by 10% from the baseline.

As shown in Table 3, the risk factors related to the improvement of one antibody titer were L-T4 doses (OR = 1.006, $p = 0.008$) and group B/group A (OR = 0.198, $p = 0.021$) and that of two antibody titers improvement were L-T4 doses (OR = 1.005, $p = 0.007$) and group B/group A (OR = 0.185, $p = 0.008$). In other words, when compared with group A, group B was a protective factor for the improvement of Hashimoto's thyroiditis antibody titer. It can be seen that the therapeutic effect of integrated TCM and L-T4 on Hashimoto's thyroiditis patients was obvious.

3.4. Analysis of Sleep Quality and Cytokine Levels. Before treatment, the PSQI and HAMA scores in group A and group B were no statistical differences, $p > 0.05$. After intervention, the PSQI in group B decreased to 4.66 ± 2.31, while that in group A was 8.80 ± 4.62, $p < 0.05$. Similarly, HAMA dropped to 6.25 ± 2.70 in group B and 8.83 ± 5.06 in group A, $p < 0.05$ (shown in Table 4). A marked decline of PSQI and HAMA scores in group B after treatment compared with before was found by the paired t test. The results

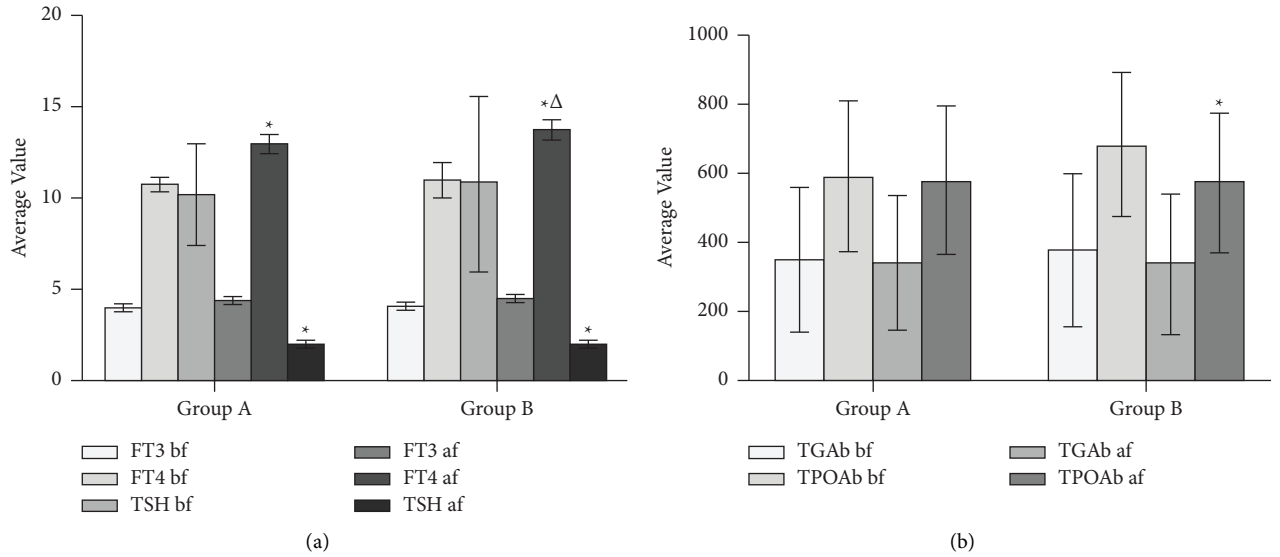

Figure 2: (a) bf: before; af: after. FT3, FT4 (pmol/L), TSH (mIU/L) compared with that before treatment of the two groups, $^{*}p < 0.05$. FT3, FT4, TSH compared with that after treatment of group A $^{\triangle}p < 0.05$. (b) TGAb, TPOAb (IU/mL) compared with that before treatment of group B $^{*}p < 0.05$.

Table 3: Analysis of risk factors related to the improvement of the antibody titer.

	Improvement of one		Improvement of two	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Sex	1.567 (0.213, 11.514)	0.659	1.278 (0.225, 7.263)	0.782
Age	1.006 (0.968, 1.046)	0.762	1.027 (0.982, 1.075)	0.241
L-T4 doses	1.006 (1.002, 1.011)	0.008**	1.005 (1.001, 1.008)	0.007**
Group B/group A	0.198 (0.050, 0.787)	0.021*	0.185 (0.053, 0.644)	0.008**

The antibody titer decreased by 10% compared with the baseline, indicating the treatment was improved, $^{*}p < 0.05$, $^{**}p < 0.01$.

Table 4: Comparison of cytokine levels before and after treatment.

Project	Category	Before		*P*	After		*P*
		Group A	Group B		Group A	Group B	
Sleep quality	PSQI	8.70 ± 4.93	8.03 ± 4.06	0.539	8.80 ± 4.62	$4.66 \pm 2.31^{\#\triangle}$	0.001
	HAMA	10.20 ± 4.73	10.94 ± 4.98	0.523	8.83 ± 5.06	$6.25 \pm 2.70^{\#\triangle}$	0.011
Cytokines (ng/ml)	IL-17A	7.970 ± 1.60	8.488 ± 1.48	0.447	6.393 ± 1.03	$4.99 \pm 1.44^{\#\triangle}$	0.001
	IFN-γ	1.423 ± 0.09	1.425 ± 0.14	0.256	$0.975 \pm 0.22^{*}$	$0.650 \pm 0.21^{\#\triangle}$	0.042
	IL-6	33.19 ± 6.13	35.65 ± 3.47	0.199	32.26 ± 4.38	$26.49 \pm 4.89^{\#\triangle}$	0.008
	IL-10	89.20 ± 14.68	71.45 ± 14.48	0.480	155.74 ± 14.24	$182.65 \pm 13.27^{\#}$	0.544

Note. Compared with that before treatment of group A, $^{*}p < 0.05$; compared with that before treatment of group B, $^{\#}p < 0.05$; compared with that after treatment of group A, $^{\triangle}p < 0.05$.

revealed that integrated TCM and L-T4 could effectively improve the sleep quality and anxiety of Hashimoto's thyroiditis patients.

As can be seen from Table 4, the cytokine levels of IL-17A, IFN-γ, IL-6, and IL-10 were no statistical differences at the baseline, $p > 0.05$. When after treatment, the levels of proinflammatory factors in group B were lower than those in group A, $p < 0.05$. While as an anti-inflammatory cytokine, the level of IL-10 was increased, although there was no significance between the two groups. Besides, through the paired *t* test, all the cytokines in group B had dramatically changed compared with those before treatment, $p < 0.05$, indicating that "Shu Gan Qing Huo Decoction" can alleviate the inflammation of Hashimoto's thyroiditis patients.

3.5. mRNA Expressions of Cytokines in Thyroid Tissues. For Hashimoto's thyroiditis with solid nodules of more than 1 cm, according to the 2020 Chinese guidelines for ultrasound malignant risk stratification of thyroid nodules (C-TIRADS), fine-needle aspiration biopsy (FNAB) was performed for the patients with C-TIRADS grading 3 and above

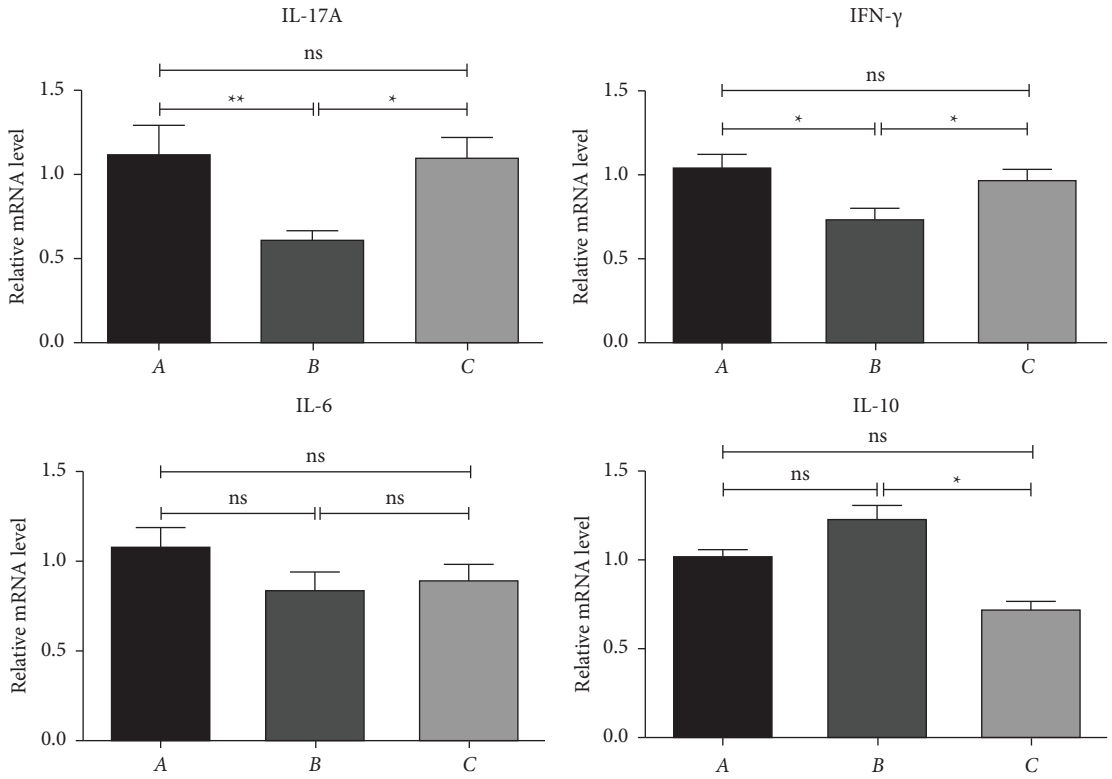

Figure 3: Relative mRNA expression levels of IL-17A, IFN-γ, IL-6, and IL-10 in fine-needle aspiration biopsy, $^{**}p < 0.01$, $^{*}p < 0.05$, ns: no significance.

who were willing to undergo. After treatment of 3 months, 12 patients (4 men and 8 women) were recruited in group A (A, $n = 12$) and 11 patients (2 men and 9 women) in group B (B, $n = 11$). 12 of the 196 patients (2 men and 10 women) before treatment were taken as the control group (C, $n = 12$). The pathological diagnosis of all the patients was Hashimoto's thyroiditis or combined with nodular goiter.

The real-time qPCR results of FNAB are revealed in Figure 3. The expression levels of IL-17A and IFN-γ in group B were much lower than those in group A and C, $p < 0.05$. On the contrary, as a protective cytokine, the level of IL-10 after treatment with TCM and L-T4 was higher than group A ($p > 0.05$) and C ($p < 0.05$). However, it was found that the expressions of the four cytokines in comparison between groups A and C were of no significance. It was further proved from histology that integrated treatment with TCM played an important role on improving the inflammation of Hashimoto's thyroiditis.

4. Discussion

In view of the complexity of HT pathogenesis, human beings have not yet recognized the essence of HT. Recent studies have shown that HT development depends on an immune defect in an individual with genetic susceptibility together with environmental factors [2]. Unfortunately, there is still a lack of effective therapeutic drugs for HT. Although thyroid function can be rectified by L-T4, it had no effect on autoantibodies, which can also be proved by our study. The use of the traditional Chinese medicine "Shu Gan Qing Huo Decoction" confirmed that the integrated treatment could effectively reduce the titers of TGAb and TPOAb in Hashimoto's thyroiditis patients with subclinical and clinical hypothyroidism, $p < 0.05$.

Bossowski and Otto Buczkowska pointed out that serum anti-thyroid antibodies, especially anti-TG and anti-TPO, and more rarely TSH stimulation blocking antibody (TSBAb), were positively correlated with the increase of thyroiditis and the development of hypothyroidism [3]. TGAb and TPOAb can directly or synergistically participate in the autoimmune response of thyroid tissues. There was evidence that TGAb and TPOAb levels were significantly correlated with the degree of cell infiltration in HT thyroiditis and HT low-density imaging detected by ultrasound [12]. Therefore, TGAb and TPOAb have become characteristic clinical markers of HT. Previous studies have reported that TCM treatment can notably decrease thyroid antibodies, as well as reduce goiter [4, 13]. It can be seen in our results that the TCM group was a protective factor for the improvement of Hashimoto's thyroiditis antibody titers. We have reason to speculate that prolonging the treatment time of TCM and L-T4 may have a more obvious effect on Hashimoto's thyroiditis.

In addition, researchers have found that the incidence of HT was related to Th17 cells [14], and the transforming growth factor (TGF)-β, IL-6, IL-10, and IFN-γ all played a promoting role in the differentiation and formation of Th17 [15, 16]. In the study, the analysis of cytokines by

ELISA from patient serum revealed that after combining with TCM treatment, the proinflammatory factors decreased significantly when compared with the L-T4 group and before, $p < 0.05$. Similar results were obtained in histology by RT-PCR detection from FNAB and strongly suggested that "Shu Gan Qing Huo Decoction" can alleviate the inflammation of Hashimoto's thyroiditis patients.

As a secondary end point, the curative effect standard of TCM syndrome was assessed in our study. We can see from Table 2 that all symptoms were improved after integrating TCM, except for poor memory, $p < 0.05$. In addition, we investigated the PSQI and HAMA before and after medication. PSQI questionnaire contained seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction [7]. The score range of each question was 0–3 in PSQI and 0–4 in HAMA. The results showed that the scores of both questionnaires in the TCM treatment group were apparently lower than the L-T4 treatment group and baseline, $p < 0.05$. The PSQI score even increased after intervened with L-T4 alone, although no statistical significance, indicating that TCM treatment had a certain role on improving patients' sleep quality and mood.

Combination treatment can comprehensively regulate the local lesions and systemic symptoms of patients, making up for the asynchronous phenomenon of functional and immune relief caused by the single use of L-T4. However, there were some limitations in our study. Firstly, as a prospective study, the intervention course was only 12 weeks due to case dropout and loss of follow-up; thus, the evaluation of long-term efficacy of TCM may not be as expected. Secondly, there were various clinical examination errors caused by multiple individuals and multiple batch tests in this study, which may lead to low statistical power. Thirdly, because of different compliance, it was not possible to ensure that each patient followed our instructions to take the medications, and we needed to expand the sample size as much as possible. Fourthly, the number for FNAB was relatively small, making it difficult to avoid biased experimental results and inadequate analysis.

5. What Is New and Conclusion

In conclusion, our study revealed that integrated treatment of TCM and L-T4 had a significant effect on thyroid autoantibodies, inflammation, and sleep quality in Hashimoto's thyroiditis patients. It was drafted with reference to the guiding principles for clinical research of new Chinese medicine (trial) [11]. Significant effect: symptoms basically disappeared, signs basically returned to normal, serum TSH level, and anti-thyroid autoantibodies were close to normal; Effective: the symptoms were significantly improved, the related signs such as goiter were alleviated, and the serum TSH level and anti-thyroid autoantibody examination were improved; ineffective: symptoms and signs are not improved, the serum TSH level is increased or decreased, and anti-thyroid autoantibodies are not changed or increased. The total effective rate of clinical efficacy in the TCM group was superior to the control group, $p < 0.05$, providing a new method for the disease treatment.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

Xudan Lou and Yuxin Huang analyzed the data regarding the thyroid diseases and contributed equally to this work. Xudan Lou was the major contributor in writing the manuscript. Jieyuzhen Qiu made statistical analysis, and Jiao Sun and Qin Gu were responsible for data collection. Haidong Wang performed the basic experiments of ELISA and real-time PCR. Xiaoming Tao and Cuiping Jiang designed and funded the study, respectively. All authors read and approved the final manuscript.

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