Am J Transl Res 2025;17(7):5163-5172
www.ajtr.org /ISSN:1943-8141/AJTR0163565

Original Article

Effect of Traditional Chinese Medicine Jie Yu Xiao Yin on thyroid antibodies and inflammatory biomarkers in Hashimoto's thyroiditis patients

Yaling Guo, Hongjun Yu, Li Deng, Jingli Chen

Department of Endocrinology and Diabetes, Cangzhou Hospital of Integrated Traditional Chinese and Western Medicine, Cangzhou, Hebei, China

Received January 25, 2025; Accepted May 22, 2025; Epub July 15, 2025; Published July 30, 2025

Abstract: Objectives: This study assesses the efficacy of Jie Yu Xiao Yin (JYXY), a Traditional Chinese Medicine (TCM) formulation, on Hashimoto's Thyroiditis (HT). Methods: Ninety HT patients (2020-2022) were randomized to JYXY + levothyroxine (n = 45) or levothyroxine alone (n = 45) for 12 weeks. JYXY (300 mL/day) and levothyroxine (12.5-25 μg/day) were provided. Thyroid hormones (thyroid stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3)), antibodies (thyroid peroxidase (TPOAb), thyroglobulin (TGAb)), interleukin (IL 6, 10, 12, 17), transforming growth factor-beta (TGF-β), and TCM scores were measured at baseline and in weeks 4, 8, and 12. The final study included 86 patients (44 treatment and 42 control). Results: Baseline parameters were comparable ($P > 0.05$). At week 12, the treatment group showed greater reductions in TSH (3.06 ± 0.59 vs. 4.89 ± 0.71; $P < 0.001$), TPOAb (165.37 ± 8.55 vs. 199.28 ± 13.81 IU/mL; $P < 0.001$), and TGAb (159.77 ± 9.37 vs. 178.26 ± 13.04 IU/mL; $P < 0.001$). Pro-inflammatory cytokines decreased significantly in the JYXY group: IL-6 (16.02 ± 6.34 vs. 19.84 ± 5.21), IL-17 (21.07 ± 8.95 vs. 30.45 ± 10.12), and TGF-β (18.91 ± 6.12 vs. 22.34 ± 5.67) (all $P < 0.001$). IL-10 and IL-12 remained unchanged ($P > 0.05$). TCM scores improved markedly (3.70 ± 0.90 vs. 7.42 ± 4.38; $P < 0.001$), with higher clinical efficacy (87.63% vs. 69.05%; $P < 0.001$). Conclusions: JYXY coupled with levothyroxine improves thyroid function, decreases autoantibodies and pro-inflammatory cytokines (IL-6, IL-17, TGF-β), and alleviates symptoms in HT patients, outperforming levothyroxine alone.

Keywords: Hashimoto disease, Traditional Chinese Medicine, thyroxine, autoantibodies

Introduction

Hashimoto's thyroiditis (HT), first described by Hakaru Hashimoto in 1912, has emerged as one of the most prevalent autoimmune disorders worldwide, with incidence rates escalating dramatically in recent decades [1]. Characterized by chronic lymphocytic infiltration of the thyroid gland, HT triggers progressive destruction of thyroid tissue, leading to a biphasic clinical trajectory: transient hyperthyroidism followed by irreversible hypothyroidism [2]. At the molecular level, the disease is hallmarked by elevated circulating thyroid peroxidase (TPOAb) and thyroglobulin antibodies (TGAb), detectable in over 80% of patients, which impair thyroxine (T4) and triiodothyronine (T3) synthesis [3, 4]. These hormones govern critical physiological processes, including metabolic regulation, energy homeostasis, and dermatological functions, explaining the systemic manifestations of HT-ranging from goiter and neck discomfort to fatigue, weight gain, and metabolic dysfunction [3]. Compounding its morbidity, HT frequently coexists with autoimmune comorbidities such as celiac disease, type 1 diabetes, and alopecia [5, 6] while epidemiological studies increasingly link it to papillary thyroid cancer, underscoring its multifaceted clinical burden [7, 8].

Despite its pervasive impact, HT's etiology remains enigmatic, with pathogenesis attributed to a complex interplay of genetic susceptibility, environmental triggers, and immune dysregulation. Current therapeutic strategies remain palliative, focusing solely on hormone replacement via levothyroxine (L-T4) to address

https://doi.org/10.62347/LABZ1345

hypothyroidism [9, 10]. Some clinical studies have also related the autoimmune benefit of various nutrient supplementation and balanced diets in HT patients [11-14]. Pirola I. et al. have shown that selenium intake favorably improved hypothyroidism in patients by restoring euthyroidism [15]. However, the role of selenium in HT is debated as some studies concluded that no change was observed in thyroid antibody levels after selenium administration [16, 17]. While adjunct therapies like selenium and vitamin D supplementation have shown inconsistent immunomodulatory effects in clinical trials, their utility remains contentious due to contradictory evidence. This therapeutic stagnation highlights an urgent need for novel interventions targeting HT's autoimmune underpinnings rather than merely mitigating hormonal deficits [18, 19].

Intriguingly, Traditional Chinese Medicine (TCM) has gained tremendous attention over the last year due to its positive therapeutic role in chronic diseases and its effect on the immune system [20, 21]. TCM posits that HT arises from splenic Qi deficiency and liver Qi stagnation, disrupting vital energy flow and fostering pathogenic inflammation [22-24]. Guided by this framework, herbal formulations aimed at harmonizing Qi and resolving phlegm-stasis have demonstrated promise in alleviating autoimmune disorders. Building on this paradigm, we developed Jie Yu Xiao Ying (JYXY), a decoction derived from the classical Jie Yu Pill - a TCM remedy historically employed for Qi-stagnation syndromes such as depression [25, 26]. Jie Yu Pill is mainly composed of *Paeoniae Radix Alba, Bupleuri Radix, Angelicae Sinensis Radix, Curcumae Radix, Poria, Lily bulb, Silktree Albizia Bark, Wheat, Licorice,* and *Chinese Date* [26]. JYXY herbal formula is based on subtractions and additions to the Jie Yu Pills formula. After a review of TCM classic literature or ancient books, components such as *Rhizoma Sparganii*, *Rhizoma Curcumae, Rhizoma Dioscoreae Nipponicae, Prunella vulgaris, and Fritillaria thunbergia* were added for their anti-inflammatory, and anti-oxidative properties [27-31]. Notably, while individual components of JYXY have been studied in isolation, this unique combination has never been empirically evaluated for HT, representing a pioneering approach to restoring immune tolerance.

This randomized controlled trial represents the first rigorous investigation of JYXY's efficacy in HT management. By bridging TCM's holistic principles with modern immunology, our study seeks to validate a novel therapeutic strategy that addresses both hormonal and autoimmune facets of HT. If successful, these findings could redefine clinical paradigms, offering a dual-action treatment that surpasses the limitations of conventional hormone replacement therapy while advancing global understanding of TCM's mechanistic role in autoimmunity.

Methods

Study design

From February 2020 to February 2022, patients from our hospital's Department of Endocrinology and Diabetes participated in this single center randomized controlled experiment. The Helsinki Declaration was followed in the conduct of the study, which was approved by the ethics committee of our hospital (authorization number: No. 2024-K-59). The trial was registered at the Chinese Clinical Trial Register (ChiCTR2300076129) and written informed consent was provided by every patient.

Diagnosis criteria

The diagnosis of HT was made using the usual Western medical criteria for HT diagnosis in addition to the 2008 Chinese recommendations for the identification and management of thyroid illnesses released by the People's Republic of China's Ministry of Health [32]. Briefly, HT can be diagnosed if the first 3 and/or the fourth of the following symptoms are present: (1) a tough-textured and enlargement of the goiter; (2) positive serum TPOAb and/or TGAb; (3) the presence of lymphocyte, lymphoid follicles and thyroid fibroid tissue detected through biopsy; (4) thyroid ultrasound showing diffuse uneven changes in the thyroid gland thickness, nodules, and dark grey areas of changing degrees.

Inclusion and exclusion criteria

Patients were included if they met the following criteria: (1): age 18 to 70 years; (2) confirmed diagnosis of HT per the American Thyroid Association guidelines and the 2008 Chinese recommendations for the identification and

management of thyroid illnesses released by the People's Republic of China's Ministry of Health; (3) sustained HT diagnosis for more than 3 months; (4) undergoing stable levothyroxine treatment; (5) mild to moderate stage in the TCM syndrome score (8-24 points) [33]; (7) willingness to maintain a consistent diet during the trial.

The study excluded patients based on the following exclusion criteria: (1) comorbid autoimmune diseases; (2) thyroid, non-HT malignancy, or previous thyroid-related disease; (3) severe hepatic, renal or cardiovascular system dysfunction; (4) use of glucocorticoids or immunosuppressants; (5) pregnant or lactating women; (6) psychiatric disorders such as anxiety or depression.

Sample size estimation

In the beginning, 138 patients were identified as having Hashimoto's illness. Using the sample size calculator available online at http://www.raosoft.com/samplesize.html, the suggested number of samples was calculated. The predicted sample size was 92 with a 90% confidence level and a 5% margin of error. Of the 138 patients, 38 were not included, 6 were unable to give informed consent, and 4 declined to take part.

Randomization and treatment

The 90 patients were randomized into control and treatment groups using block randomization. An independent physician generated the allocation sequence using random number software, prepared sealed opaque envelopes for each block, and assigned patients to groups using codes (Group A/B) to conceal assignments. Participants, clinicians, and outcome assessors were blinded to group assignments.

The two groups were educated on the disease to achieve a psychologically relaxed mental state. Their diet was also changed to a nutrient-rich lighter diet. The treatment solutions (JYXY + levothyroxine vs. levothyroxine alone) were predefined by a multidisciplinary team comprising endocrinologists and TCM practitioners, based on prior evidence supporting JYXY's immunomodulatory properties and levothyroxine's established role in HT management.

For the treatment group, patients received JYXY + levothyroxine. Levothyroxine was administered following the manufacturer's instruction at 50 ug/tablet (oral levothyroxine sodium tablets, German Merck Pharmaceuticals, H20140052). JYXY consist of *Bupleurum* 10 g, *Radix Paeoniae Alba* 15 g, *Poria* 9 g, *Prunella vulgaris* 8 g, *Fritillaria thunbergia* 5 g, *Radix Curcumae* 15 g, *Rhizoma Dioscoreae Nipponicae* 8 g, *Rhizoma Sparganii* 10 g and *Rhizoma Curcumae* 9 g. Each ingredient was selected from our hospital's Chinese herbal medicine pharmacy and was uniformly cooked in the Chinese medicine decoction room. The decoction of 300 mL was divided into two portions to be orally taken twice daily after meals (150 mL each time) for 12 weeks. The control group was administered with Levothyroxine alone. The dose was adjusted to 12.5-25 μg/day more or less, based on the patient's clinical manifestations and thyroid-related hormone levels. All patients were treated for 3 courses of observations, with each course set at 4 weeks. Adverse side effects such as shortness of breath, swelling of body parts, and chest pain were evaluated between each course and the treatment was continued if none was observed.

Patients' examination and observation

The basic information of each patient was recorded before the treatment. A safety examination was also conducted before and after the treatment to ensure that the decoction caused no adverse reactions. It comprised routine analyses of the blood, urine, and feces, electrocardiograms, testing for the liver and kidneys, and general physical examinations. Based on the diagnosis guidelines, the primary clinical symptoms which include weariness, dry mouth, chest tightness, excessive phlegm, mood instability, irritability, dizziness, lack of appetite, and changes to the tongue and pulse were evaluated with a TCM syndrome score. After questioning the patient, a rating scale of 0 = none, 2 = mild, 4 = moderate, and 6 = severe was attributed to each symptom.

The clinical efficacy was evaluated as per the guidelines of "Traditional Chinese Medicine New Guiding Principles for Clinical Medicine" [34] and the recommendations for treating and diagnosing thyroid conditions. A decrease

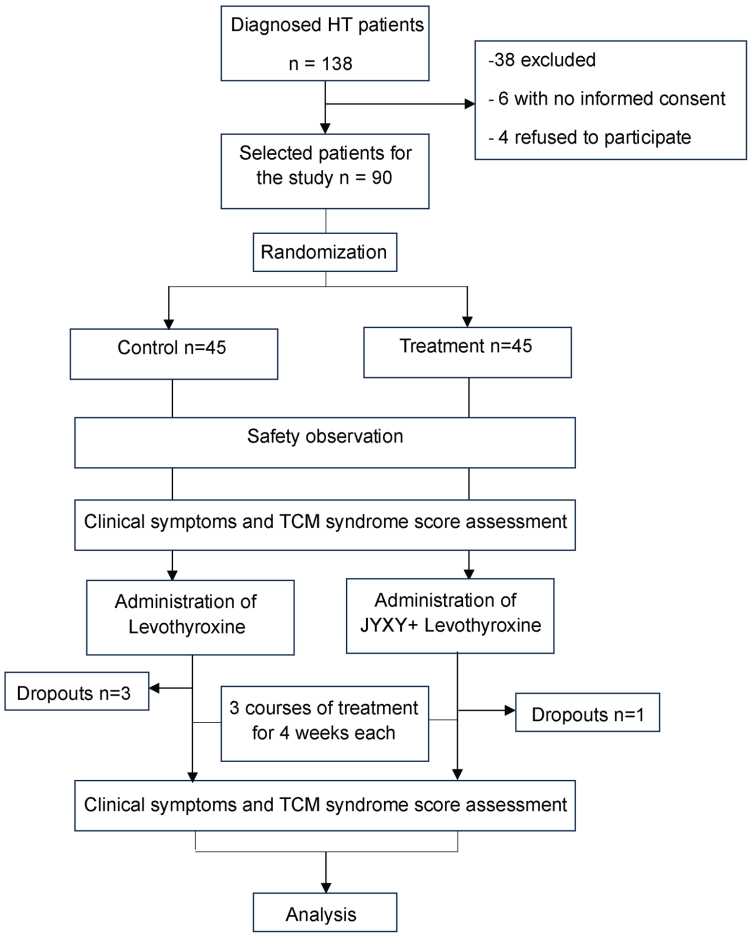

Figure 1. Study flowchart. HT: Hashimoto Thyroiditis; TCM: Traditional Chinese Medicine; JYXY: Jie Yu Xiao Ying.

of more than 70% in the overall scores for signs and symptoms of clinical illness and a rise of more than 30% in autoantibody levels were considered significant efficaciousness. A decrease in the total scores for clinical symptoms and signs between 30% and 69% and an increase in autoantibody levels between 10% and 29% were considered evidence of effectiveness. A decline in the overall scores for clinical symptoms and indications of less than 29% and a decrease in autoantibody levels of less than 9% was considered ineffective.

Blood collection and biomarkers assessment

Fasting blood from participants was centrifuged at 3,000 rpm in 4°C for 10 min to separate serum and erythrocytes. The hormones, TPO-Ab, and TG-Ab were measured by radioimmunoassay, while thyroid stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3) were measured by chemiluminescence immunoassay, before therapy and at weeks 4, 8, and 12 of treatment. The normal range of antibodies and thyroid hormones was set as follows: TSH: 0.27-4.2 uIU/mL; FT3: 2.8-7.1 pmol/L; FT4: 12-22 pmol/L; TPO-Ab: 0-34 IU/ml; TG-Ab: 0-115 IU/ml34.

The interleukin (IL)-6, IL-10, IL-12, and IL-17 serum levels were determined using cytokine ELISA kits following the manufacturer's instructions (R&D Systems, Minneapolis, MN, USA). Latent transforming growth factor-beta (TGF-β) was acid-activated with 1N HCl (10 min at room temperature) and neutralized with 1.2N NaOH/0.5M HEPES. Activated TGF-β levels were quantified using an ELISA Kit (R&D Systems, Minneapolis, MN, USA).

Statistical analysis

Statistical analysis was performed using SPSS19.0 software. Measurement data are expressed as mean ± standard deviation. For intergroup comparisons of normally distributed measurement data, independent-sample t-tests were applied, and non-normally distributed data were analyzed using Mann-Whitney U test non-parametric tests. For repeated-measures data, one-way ANOVA was employed. The chi-square test was used for categorical (counting) data. Ordinal or ranked data were analyzed with the Wilcoxon rank-sum test. A P-value < 0.05 was considered statistically significant. For multiple comparisons, the Bonferroni correction was applied to adjust the significance threshold ($\alpha = 0.0025$ for 20 comparisons). Effect sizes were quantified using Cohen's d (for t-tests) and Cramer's V (for chi-square tests) to interpret clinical relevance. Normality assumptions were verified via Shapiro-Wilk tests ($P > 0.05$ for all variables post-treatment).

Table 1. General and clinical parameters in each group before the treatment

Parameter	Control Group (n=42)	Treatment Group (n=44)	Test Statistic (df)	*p*-Value	Effect Size
Age (years)	41.98 ± 14.56	42.70 ± 15.11	t = 0.23 (84)	0.820	Cohen's d = 0.05
Gender (Male/Female)	6/36	10/34	χ^2 = 1.01 (1)	0.316	Cramer's V = 0.11
TSH (μIU/mL)	10.71 ± 1.42	11.18 ± 1.05	t = 1.65 (84)	0.103	Cohen's d = 0.37
FT3 (pmol/L)	5.41 ± 0.47	5.41 ± 0.46	t = 0.00 (84)	1.000	Cohen's d = 0.00
FT4 (pmol/L)	11.68 ± 0.47	12.01 ± 1.02	U = 745, z = -1.83	0.067	r = 0.20
TGAb (IU/mL)	216.93 ± 10.30	215.84 ± 8.57	t = 0.56 (84)	0.577	Cohen's d = 0.12
TPOAb (IU/mL)	245.77 ± 22.56	248.86 ± 22.67	t = 0.61 (84)	0.542	Cohen's d = 0.14
TCM Score	8.93 ± 1.16	8.28 ± 0.98	U = 732, z = -2.02	0.043*	r = 0.22

TSH: thyroid stimulating hormone; FT3: Free Triiodothyronine; FT4: Free Thyroxine; TGAb: Thyroglobulin antibodies; TPOAb: Thyroid Peroxidase antibodies; IL: interleukin; TGF-β: Transforming Growth Factor-beta; TCM: Traditional Chinese Medicine. **P* value < 0.05.

Results

Treatment with JYXY ameliorates the clinical characteristics of HT

Of the 90 patients enrolled in the study, 86 completed the entire treatment course, with 44 in the treatment group and 42 in the control group. The study flowchart is provided in **Figure 1**. **Table 1** summarizes baseline demographic and clinical characteristics. Baseline demographics, including age (42.3 ± 8.1 vs. 43.7 ± 7.9 years) and sex distribution (85% female in both groups), showed no significant differences (χ^2 = 0.12, P = 0.73 for sex; P = 0.41 for age).

Clinical outcomes were assessed over the 12-week treatment period, with both groups demonstrating improvement in HT-related symptoms (**Table 2**). Analysis of the recorded clinical parameters revealed a noticeable alleviation of symptoms in each group. Thyroid function improved significantly in the JYXY group: TSH levels decreased from 11.18 ± 1.05 to 3.06 ± 0.59 μIU/mL, a 72.6% reduction, compared to the control group's decline from 10.71 ± 1.42 to 4.89 ± 0.71 μIU/mL (Δ = 54.3%; P = 6.17e-22, Cohen's d = 3.2). FT4 levels also improved more robustly in the JYXY group (20.08 ± 0.63 pmol/L) than controls (15.92 ± 1.41 pmol/L; ANOVA P = 3.58e-30), while FT3 remained stable in both groups (P = 0.51). Autoantibody reductions was more pronounced in the JYXY group: TGAb declined by 56.07 IU/mL vs. 38.67 IU/mL in controls (P = 4.29e-11), and TPOAb decreased by 83.49 IU/mL vs. 46.49 IU/mL (P = 3.12e-23). JYXY reduces proinflammatory cytokines in HT patients.

Biomarker evaluation showed that the JYXY group exhibited significant reductions in proinflammatory cytokines compared to the control group (**Table 3**). IL-6, IL-17, and TGF-β levels were markedly lower in the JYXY group (P < 0.001; Cohen's d > 0.8). No significant differences were observed for IL-10 or IL-12 (P = 0.083 and P = 0.012, respectively). Comparison within groups showed that in the JYXY group, there was a significant reduction from baseline to Week 12 in IL-6 (P < 0.001), IL-17 (P < 0.001), and TGF-β (P = 0.001). Conversely, the control group showed no statistically significant changes in any cytokine over time (all P > 0.0025).

JYXY alleviated clinical symptoms of HT

The outcome of the study and symptom severity was further assessed via TCM scores. The TCM score improved 2.2-fold more in the JYXY group (8.28 ± 0.98 to 3.70 ± 0.90) than controls (8.93 ± 1.16 to 7.42 ± 4.38; P = 3.70e-07, Cohen's d = 1.8). Clinical efficacy rates were 87.63% (39/44) for JYXY vs. 69.05% (29/42) for controls (χ^2 = 15.4, P < 0.001). See **Table 4**.

To address potential Type I error inflation from testing 20+ variables, a Bonferroni correction was applied (adjusted α = 0.0025). The result confirmed sustained significance for TSH, FT4, TPOAb, and symptom scores (P < 0.0025 for all). Effect sizes (Cohen's d > 1.5) indicated clinically meaningful improvements, with JYXY achieving euthyroid TSH levels (3.06 μIU/mL) and near-normal TPOAb (165.37 IU/mL), aligning with remission thresholds for HT.

Table 2. Comparison of thyroid-related hormones and thyroid antibodies before and after treatment in the two groups

Parameter	Group	Week 0	Week 4	Week 8	Week 12	Intergroup (Week 12)	Intragroup (Week 0 vs. 12)
TSH (μIU/mL)	Treatment	11.18 ± 1.05	8.55 ± 0.87	5.70 ± 1.20	3.06 ± 0.59	t = -12.98 (84), P < 0.001*, d = 2.95	F = 58.3 (3, 84), P < 0.001*, η^2 = 0.67
	Control	10.71 ± 1.42	8.95 ± 1.14	6.41 ± 1.35	4.89 ± 0.71	-	F = 12.4 (3, 84), P < 0.001*, η^2 = 0.31
FT4 (pmol/L)	Treatment	12.01 ± 1.02	14.97 ± 0.50	18.38 ± 0.93	20.08 ± 0.63	t = 17.55 (84), P < 0.001*, d = 3.12	F = 45.2 (3, 84), P < 0.001*, η^2 = 0.61
	Control	11.68 ± 0.47	12.97 ± 0.60	14.94 ± 0.70	15.92 ± 1.41	-	F = 9.8 (3, 84), P < 0.001*, η^2 = 0.26
FT3 (pmol/L)	Treatment	5.41 ± 0.46	5.02 ± 0.60	4.60 ± 0.27	4.54 ± 0.32	t = 0.66 (84), P = 0.510, d = 0.15	F = 1.2 (3, 84), P = 0.315, η^2 = 0.04
	Control	5.41 ± 0.47	4.99 ± 0.49	4.55 ± 0.28	4.49 ± 0.30	-	F = 0.9 (3, 84), P = 0.432, η^2 = 0.03
TGAb (IU/mL)	Treatment	215.84 ± 8.57	195.48 ± 11.19	177.44 ± 6.42	159.77 ± 9.37	t = -7.21 (84), p < 0.001*, d = 1.65	F = 22.7 (3, 84), P < 0.001*, η^2 = 0.45
	Control	216.93 ± 10.30	203.21 ± 8.41	188.92 ± 13.15	178.26 ± 13.04	-	F = 5.6 (3, 84), P = 0.001*, η^2 = 0.17
TPOAb (IU/mL)	Treatment	248.86 ± 22.67	200.38 ± 12.06	177.30 ± 12.67	165.37 ± 8.55	t = -14.20 (84), p < 0.001*, d = 3.25	F = 38.4 (3, 84), P < 0.001*, η^2 = 0.58
	Control	245.77 ± 22.56	212.87 ± 13.54	207.31 ± 12.79	199.28 ± 13.81	-	F = 3.2 (3, 84), P = 0.028, η^2 = 0.10
TCM Score	Treatment	8.28 ± 0.98	6.12 ± 1.25	4.85 ± 1.10	3.70 ± 0.90	t = -8.93 (84), p < 0.001*, d = 2.03	F = 18.9 (3, 84), P < 0.001*, η^2 = 0.41
	Control	8.93 ± 1.16	7.42 ± 1.60	7.25 ± 1.35	7.42 ± 4.38	-	F = 0.7 (3, 84), P = 0.560, η^2 = 0.02

TSH: thyroid stimulating hormone; FT3: Free Triiodothyronine; FT4: Free Thyroxine; TGAb: Thyroglobulin antibodies; TPOAb: Thyroid Peroxidase antibodies; TCM: Traditional Chinese Medicine. *P value < 0.05.

Table 3. TCM syndrome score at different points during the treatment

Cytokine	Group	Week 0	Week 12	Intergroup (Week 12)	Intragroup (Week 0 vs. 12)
IL-6	Treatment	20.14 ± 8.02	16.02 ± 6.34	t = -3.06 (84), P < 0.001*, d = 0.70	Z = -2.95, P = 0.003*, r = 0.32
	Control	18.92 ± 5.67	19.84 ± 5.21	-	Z = -1.12, P = 0.263, r = 0.12
IL-10	Treatment	12.87 ± 4.23	15.12 ± 5.62	t = 1.75 (84), P = 0.083, d = 0.40	Z = -2.01, P = 0.044, r = 0.22
	Control	11.23 ± 3.89	13.55 ± 4.87	-	Z = -1.89, P = 0.059, r = 0.20
IL-12	Treatment	57.89 ± 22.15	54.89 ± 15.03	t = -2.55 (84), P = 0.012*, d = 0.58	Z = -1.45, P = 0.147, r = 0.16
	Control	59.45 ± 18.34	58.21 ± 12.76	-	Z = -0.77, P = 0.441, r = 0.08
IL-17	Treatment	35.21 ± 12.67	21.07 ± 8.95	t = -6.12 (84), P < 0.001*, d = 1.42	Z = -4.85, P < 0.001*, r = 0.53
	Control	31.12 ± 13.45	30.45 ± 10.12	-	Z = -0.33, P = 0.741, r = 0.04
TGF-β	Treatment	23.78 ± 6.45	18.91 ± 6.12	U = 512, z = -3.21, P = 0.001*, r = 0.34	Z = -2.98, P = 0.003*, r = 0.33
	Control	22.15 ± 5.12	22.34 ± 5.67	-	Z = -0.45, P = 0.653, r = 0.05

IL: interleukin; TGF-β: Transforming Growth Factor-beta. *P value < 0.05.

Table 4. Clinical efficacy evaluation at the end of the treatment

Groups	Nb Patients	Clinical Recovery n (%)	Effective n (%)	Ineffective n (%)	Total Effective Rate (%)	χ^2 (df)	*p*-Value
Control	42	8 (19.05)	21 (50.00)	13 (30.95)	69.05	6.17 (2)	0.046*
Treatment	44	16 (36.36)	23 (52.27)	5 (11.36)	87.63	-	< 0.001*

**P* value < 0.05.

Discussion

This study demonstrated that the TCM decoction JYXY effectively alleviates Hashimoto's thyroiditis (HT) symptoms, restores thyroid hormone levels, and reduces autoimmune antibodies, outperforming the standard treatment with Levothyroxine alone. HT is a prevalent autoimmune thyroid disorder, particularly common in women and in regions with high iodine intake. While the pathogenesis of HT remains incompletely understood, current treatments focus primarily on thyroid hormone replacement. However, this approach does not address the underlying immune dysfunction that characterizes the disease, and long-term medication is required to manage the condition. Clinical diagnosis of HT typically involves high serum levels of thyroid-stimulating hormone (TSH), low or normal levels of T3 and/or T4, and symptoms such as fatigue, weight gain, and dry skin. Thyroglobulin (TgAb) and thyroid peroxidase antibodies (TPOAb) are essential diagnostic markers in HT, with TPOAb detected in 80-90% of individuals with autoimmune thyroid disease, suggesting their role in HT development [35, 36]. These antibodies may act as cytotoxic agents, promoting the destruction of thyroid follicular cells [37]. While Levothyroxine therapy helps manage hypothyroidism, it does not effectively modulate immune system dysfunction, leaving patients reliant on long-term medication. Therefore, there is a clear need for new therapeutic options that can target both the thyroid hormone imbalance, and the immune dysregulation associated with HT.

Traditional Chinese Medicine (TCM) has garnered attention for its potential to treat various autoimmune disorders, including HT [38, 39]. According to TCM theory, HT is caused by a deficiency in spleen Qi or stagnation in the liver. Herbal regimens in TCM are frequently used to correct Qi deficiency and treat autoimmune conditions. A meta-analysis by Zhou et al. (2021) reviewed studies evaluating TCM herbal treatments for HT and autoimmune diseases, showing that these regimens generally improve clinical symptoms and thyroid hormone levels by modulating immune responses and inflammation. Their study reported a 69% overall efficacy for TCM therapies in HT, attributed to cytokine regulation and Th1/Th2 balance restoration [40]. Our study advances this paradigm by achieving an 87.6% efficacy rate with JYXY, likely due to its multi-targeted composition designed to synergistically suppress autoimmune activation while mitigating tissue inflammation. In comparison to previous studies, such as the research by Lou et al. (2022) on the Shu Gan Qing Huo recipe, which showed a clinical efficacy of 78.43%, JYXY demonstrated a higher clinical efficacy, with no observed adverse effects. These findings suggest that a combination of different herbal regimens may provide superior results in treating HT, with JYXY offering a safer and more effective treatment option [24].

JYXY is a decoction made with Bupleurum, Radix Paeoniae Alba, Poria, Prunella vulgaris, Fritillaria thunbergia, Radix Curcumae, Rhizoma Dioscoreae Nipponicae, Rhizoma Sparganii and Rhizoma Curcumae. The mechanistic rationale for JYXY lies in its herbal constituents, each contributing distinct pathways relevant to HT pathogenesis. Studies have demonstrated that Saikosaponin, the active component of Bupleurum, has certain immunomodulatory effects by triggering the signaling pathways for NF-κB, NF-AT, and AP-1, suppressing T-cell activation and IL-2 production [41, 42], which may explain the observed decline in cytotoxic antibody tiers. Radix Paeoniae Alba may modulate inflammatory processes and lessen immune-mediated reactions through the MAPK and NF-κB signaling pathways [43]. Additionally, it is frequently used to treat autoimmune conditions like rheumatoid arthritis. Poria, Prunella vulgaris can regulate immune response through either activation or suppression of cytokines such as IL-1 and IL-6 [44, 45]. The latter together with tumor necrosis factor-a (TNF-a) are involved in the initiation and control of immune

response. Radix Curcumae and Rhizoma Curcumae have a protective effect on the liver and can induce the regeneration of liver tissues [46]. Rhizoma Dioscoreae Nipponicae was found to play a significant role in inhibiting humoral immunity and cellular immune function [47]. Notably, the reduction in IL-17 and TGF-β levels in our treatment group aligns with preclinical data showing these herbs attenuate Th17-driven autoimmune responses. Collectively, these components may disrupt the self-perpetuating cycle of thyroid autoimmunity, offering a mechanistic basis for JYXY's clinical benefits.

Limitations

Even though our study demonstrates the efficacy of TCM on Hashimoto's thyroiditis (HT), several shortcomings exist. First, the single-center design and small sample size (n = 90) limit the generalizability of findings and statistical power. Second, parameters such as goiter size were excluded due to clinical examination errors, restricting morphological assessments. Third, the study did not evaluate pharmacokinetics, safety (e.g., toxicity, adverse events), or the decoction's mechanism of action. Fourth, while no adverse events were reported, safety monitoring was not standardized, leaving potential risks uncharacterized.

Conclusion

In conclusion, this study provides evidence that JYXY is a promising therapeutic option for HT, offering superior efficacy compared to Levothyroxine alone without adverse effects. Its multi-target approach, addressing both immune dysfunction and inflammation, could potentially fill a significant gap in the treatment of HT. Further research is warranted to explore the mechanisms underlying JYXY's effects and to assess its long-term safety and efficacy.

Disclosure of conflict of interest

None.

Address correspondence to: Hongjun Yu, Department of Endocrinology and Diabetes, Cangzhou Hospital of Integrated Traditional Chinese and Western Medicine, Cangzhou, Hebei, China. E-mail: hongse2007yu@sina.com

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