



Research on Clinical Efficacy and Immunomodulatory Mechanisms of an Integrated Traditional Chinese and Western Medicine Approach for Treating Chronic Cough Based on the “Concurrent Treatment of Lung and Spleen” Theory

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Abstract: *Objective:* This study aims to explore the clinical efficacy of an integrated traditional Chinese and Western medicine approach for treating chronic cough based on the “concurrent treatment of lung and spleen” theory and to conduct an in-depth analysis of its immunomodulatory mechanisms, including the balance of T lymphocyte subsets, regulation of immunoglobulin levels, and associated molecular pathways. This research seeks to provide new insights and evidence-based foundations for the clinical treatment of chronic cough. *Methods:* A total of 120 patients with chronic cough who were treated in the hospital from January 2023 to June 2024 were selected and randomly divided into an observation group and a control group using a random number table method, with 60 patients in each group. The control group received standardized Western medical treatment (budesonide/formoterol powder inhaler combined with montelukast sodium tablets), while the observation group received traditional Chinese medicine syndrome differentiation treatment based on the “concurrent treatment of lung and spleen” theory (self-formulated Yiqi Jianpi Runfei Decoction with modifications) in addition to the control group’s treatment. Both groups were treated continuously for 8 weeks. The cough symptom scores, cough visual analog scale (VAS) scores, and quality of life scores (LCQ) were compared between the two groups before and after treatment. Peripheral blood immune indicators [CD3+, CD4+, CD8+, CD4+/CD8+, immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin M (IgM)] and levels of related cytokines (IL-4, IFN- γ , TNF- α) were measured before and after treatment. The clinical efficacy and incidence of adverse reactions were statistically analyzed, and subgroup analyses were conducted based on age and disease duration. *Results:* After 8 weeks of treatment, the overall effective rate in the observation group was 93.33% (56/60), significantly higher than that in the control group, which was 76.67% (46/60), with a statistically significant difference ($P < 0.05$). Subgroup analysis revealed that the observation group demonstrated superior therapeutic effects compared to the control group across different age and disease duration subgroups ($P < 0.05$). Both groups showed a significant reduction in cough symptom scores and cough VAS scores, along with a significant increase in LCQ scores compared to pre-treatment levels. Moreover, the magnitude of improvement in the observation group was superior to that in the control group, with statistically significant differences ($P < 0.05$). Peripheral blood levels of CD3+, CD4+, CD4+/CD8+, IgG, and IgA significantly increased in both groups, while CD8+ levels significantly decreased post-treatment. The observation group exhibited a greater degree of improvement in immune indicators compared to the control group, with

statistically significant differences ($P < 0.05$). Additionally, the observation group showed a significant reduction in IL-4 and TNF- α levels and a significant increase in IFN- γ levels compared to pre-treatment, with statistically significant differences compared to the control group ($P < 0.05$). There was no statistically significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$). *Conclusion:* The integrated traditional Chinese and Western medicine approach based on the “simultaneous treatment of lung and spleen” theory demonstrates definite clinical efficacy in treating chronic cough. It significantly improves cough symptoms and quality of life in patients across different subgroups. Its mechanism of action may be related to regulating immune function, balancing T lymphocyte subsets, modulating immunoglobulin levels, and regulating relevant cytokine pathways. With good safety, this approach is worthy of clinical promotion and application.

Keywords: Simultaneous treatment of the lung and spleen; Integrated traditional Chinese and Western medicine; Chronic cough; Clinical efficacy; Immunoregulation; T lymphocyte subsets; Immunoglobulin; Cytokines

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1. Introduction

Chronic cough is a common clinical condition in respiratory departments, defined as a cough lasting for ≥ 8 weeks with no obvious abnormalities detected in chest imaging examinations. It has a relatively high incidence rate, with the global prevalence of chronic cough in adults estimated to be approximately 9% to 33%, severely impacting patients' physical and mental health as well as their quality of life^[1]. Currently, it is believed that the etiology of chronic cough is complex and closely related to airway hyperresponsiveness, chronic airway inflammation, neuroregulatory disorders, and immune dysfunction^[1]. Among these factors, immune dysfunction stands out as one of the core pathogenic mechanisms: T lymphocyte subsets, as the core of the body's immune regulation, include CD3+ representing total T lymphocytes, CD4+ as helper T lymphocytes (which promote immune responses), and CD8+ as cytotoxic T lymphocytes (which suppress immune responses). An imbalance in the CD4+/CD8+ ratio can lead to immune response disorders, thereby causing persistent airway inflammation. Immunoglobulins (IgG, IgA, IgM), as crucial components of humoral immunity, have their abnormal levels reducing airway defense functions and exacerbating chronic inflammatory responses^[2-3]. Studies have shown that in patients with chronic cough, peripheral blood CD4+ levels are significantly decreased, CD8+ levels are significantly increased, and IgG and IgA levels are lower than those in healthy individuals. Furthermore, an imbalance in the inflammatory cytokine network (increased IL-4 and TNF- α , decreased IFN- γ) further exacerbates airway damage^[4].

At present, Western medicine treatment mainly focuses on symptomatic relief, such as anti-inflammation, antispasmodic, and cough-relieving measures. Commonly used drugs include glucocorticoids and leukotriene modifiers. However, long-term use of these medications can lead to adverse reactions such as drug resistance, immunosuppression, and dysbacteriosis. Moreover, some patients experience suboptimal therapeutic effects, with recurrent and protracted conditions. Approximately 30% to 40% of patients do not show significant improvement in symptoms after undergoing pure Western medicine treatment^[5-7]. Traditional Chinese medicine (TCM) categorizes chronic cough under the realms of “prolonged cough” and “stubborn cough.” Its pathogenesis is not attributed to a single organ pathology but is closely related to the dysfunction of both the lungs and spleen. As stated in the “Huangdi Neijing” (The Yellow Emperor's Classic of Internal Medicine), “the spleen is the source of phlegm production, and the lungs are the storage organ for phlegm.” The lungs govern qi and regulate respiration, while the spleen governs the transformation and transportation of water and food essences. If spleen deficiency leads to impaired transportation, water and dampness accumulate internally, forming phlegm that ascends to obstruct the lungs, causing impaired lung function and resulting in cough. Conversely, prolonged coughing can injure the lungs, leading to insufficient lung qi, which is unable to assist the

spleen in its transportation and transformation functions, further exacerbating spleen deficiency and damp-phlegm accumulation. This creates a vicious cycle of “dual deficiency of the lungs and spleen, with damp-phlegm obstructing the lungs”^[8-9]. The TCM concept of “holism” emphasizes the collaborative role of organs. The lungs and spleen are interdependent in the generation of qi and blood, metabolism of body fluids, and immune defense. This theory is highly correlated with the immune network regulatory mechanisms in modern medicine^[10]. Therefore, the core treatment principle in TCM for chronic cough is “simultaneous treatment of the lungs and spleen.” By invigorating qi and strengthening the spleen, as well as moistening the lungs and relieving cough, this approach addresses both the root cause and the symptoms, regulating organ function from the source and improving cough symptoms.

In recent years, the integrated treatment of chronic cough with traditional Chinese and Western medicine has gradually become a research hotspot. Studies have confirmed that traditional Chinese medicine (TCM) prescriptions based on the theory of “simultaneous treatment of the lung and spleen” can improve the clinical symptoms of patients with chronic cough. However, most studies have only focused on observing therapeutic effects, with insufficient exploration of their immune regulatory mechanisms. Additionally, there is a lack of analysis on the differences in therapeutic effects among different populations (e.g., patients of different ages and disease durations)^[11-12]. Meanwhile, in current similar studies, there is insufficient elaboration on the compatibility logic and preliminary application basis of TCM prescriptions, making it difficult to fully support the scientific validity of their clinical applications^[13]. Furthermore, existing studies have rarely explored the collaborative regulatory mechanisms between cytokine networks, T lymphocyte subsets, and immunoglobulins. Moreover, some studies have small sample sizes and lack long-term follow-up data, limiting the reliability and generalizability of their conclusions^[14]. Guided by the theory of “simultaneous treatment of the lung and spleen”, this study constructs an integrated traditional Chinese and Western medicine treatment plan. By systematically observing clinical symptoms, quality of life, immune function indicators (including cytokines), and safety, combined with subgroup analysis, the study aims to clarify the efficacy and applicable population of the plan and delve into its molecular mechanisms of immune regulation. The goal is to provide a more targeted plan and theoretical support for the treatment of chronic cough.

2. Materials and methods

2.1. General information

A total of 120 patients with chronic cough who received outpatient and inpatient treatment in the respiratory department of the hospital from January 2023 to June 2024 were selected as the study subjects.

Inclusion criteria: (1) Meeting the Western medical diagnostic criteria for chronic cough, with cough duration exceeding 8 weeks and no obvious organic lesions detected by chest CT/MRI scans^[15]; (2) Meeting the diagnostic criteria for “deficiency of both lung and spleen qi, with phlegm-dampness obstructing the lung” in traditional Chinese medicine, with primary symptoms including recurrent coughing, weak cough sound, copious white and thin sputum, shortness of breath, and fatigue^[16]; secondary symptoms including poor appetite, abdominal distension and loose stools, mental and physical fatigue with reluctance to speak, pale tongue with a white and greasy coating, and a thin and slippery pulse; (3) Aged between 18 and 70 years old; (4) Not having used glucocorticoids, immunosuppressants, or other traditional Chinese medicines for relieving cough and resolving phlegm within the past week; (5) Patients being informed about the study and signing an informed consent form.

Exclusion criteria: (1) Having organic pulmonary diseases such as bronchial asthma, chronic obstructive pulmonary disease, pulmonary tuberculosis, or lung cancer; (2) Having dysfunction of vital organs such as the heart, liver, or kidneys; (3) Having immune system diseases, diabetes, or hypertension (with poorly controlled blood

pressure); (4) Being pregnant or lactating women; (5) Having allergies to the medications used in this study; (6) Having poor compliance and being unable to complete the entire course of treatment and follow-up.

A total of 120 patients were randomly divided into an observation group and a control group using a random number table method, with 60 patients in each group. In the observation group, there were 32 males and 28 females; aged between 22 and 68 years old, with an average age of (45.62 ± 8.31) years; and with a disease duration ranging from 8 to 36 weeks, with an average duration of (16.25 ± 5.17) weeks. In the control group, there were 31 male cases and 29 female cases; the age range was 20 to 69 years, with an average age of (44.85 ± 8.53) years; the disease duration ranged from 8 to 34 weeks, with an average of (15.76 ± 5.32) weeks. There were no statistically significant differences in general data (gender, age, disease duration) between the two groups ($P > 0.05$), indicating comparability.

Rationale for sample size estimation: Based on similar studies, with α set at 0.05 and β at 0.10, the overall efficacy rate of the observation group was estimated at 90%, while that of the control group was estimated at 75%^[12]. Using PASS 15.0 software, the minimum required sample size per group was calculated to be 52 cases. Considering a dropout rate of 10%, the final sample size was determined to be 60 cases per group, with a total sample size of 120 cases.

2.2. Treatment methods

2.2.1. Control group (standardized Western medical treatment)

Patients were administered budesonide/formoterol powder for inhalation (AstraZeneca AB, National Medical Products Administration Approval Number J20140047), one inhalation per dose, twice daily, followed by gargling after inhalation; combined with montelukast sodium tablets (Merck Sharp & Dohme (Hangzhou) Pharmaceutical Co., Ltd., National Medical Products Administration Approval Number J20180077), 10 mg per dose, once daily, taken orally before bedtime. The treatment was continued for 8 weeks. The combination of budesonide and montelukast sodium can synergistically inhibit airway inflammation and hyperresponsiveness, but its regulatory effect on immune function is limited, making it difficult to improve the underlying imbalance in the patient's constitution^[17].

2.2.2. Observation group (integrated traditional Chinese and Western medicine treatment)

On the basis of the treatment applied to the control group, traditional Chinese medicine (TCM) syndrome differentiation treatment based on the theory of "simultaneous treatment of the lung and spleen" was adopted, using a self-formulated Yiqi Jianpi Runfei Decoction with modifications.

Logic of Formula Compatibility: This formula takes "invigorating qi and strengthening the spleen, moistening the lung and resolving phlegm" as its core, adhering closely to the treatment principle of "simultaneous treatment of the lung and spleen." The principal drugs are Astragalus (20 g) and Codonopsis (15 g), which invigorate qi and strengthen the spleen, as well as replenish the lung and consolidate the exterior, targeting the root cause of deficiency in both the lung and spleen. The adjuvant drugs are Atractylodes (12 g) and Poria (15 g), which strengthen the spleen and remove dampness, assist the spleen in transportation and transformation, cut off the source of phlegm production, and assist the principal drugs in enhancing the spleen-strengthening effect. The assistant drugs include Tangerine Peel (10 g) and Pinellia (10 g) to regulate qi and resolve phlegm; Almond (10 g), Tatarian Aster (12g), and Stemona (12 g) to moisten the lung and relieve cough; and Platycodon (10 g) to ventilate the lung and benefit the throat, collectively achieving the effects of resolving phlegm, relieving cough, and ventilating the lung qi. The envoy drug is Roasted Licorice (6 g), which harmonizes all the drugs in the formula and takes into account the properties of the entire formula. Modern research indicates that this compatibility pattern can regulate the body's immune function through multiple targets, forming a complement to symptomatic treatment in Western medicine^[18].

Syndrome-Based Modifications: For patients with excessive and sticky phlegm, add 12 g of Thunberg Fritillary

Bulb and 15 g of Snakegourd Fruit (to clear heat, resolve phlegm, moisten dryness, and dissipate nodules); for those with obvious shortness of breath, add 6 g of American Ginseng (decocted separately, to invigorate qi and nourish yin); for those with severe abdominal distension and loose stools, add 20 g of Roasted Coicis Seed and 15 g of Roasted Chinese Yam (to strengthen the spleen, permeate dampness, and stop diarrhea); for those with a persistent cough that does not heal, add 6 g of Schisandra and 10 g of Black Plum (to astringent and consolidate, as well as to astringent the lung and relieve cough).

Decoction and administration method: Take one dose per day. Add 500 mL of water, soak for 30 minutes, and then decoct until the volume reduces to 200 mL. Administer the decoction in two divided doses, warm, in the morning and evening, continuously for 8 weeks.

Preliminary foundation of the formula: Studies have confirmed that the core drug combination in the formula (*Astragalus membranaceus*, *Codonopsis pilosula*, *Atractylodes macrocephala*, and *Poria cocos*) can significantly improve the immune function of spleen-deficiency model animals and enhance T-lymphocyte activity^[19].

2.3. Observation indicators

2.3.1. Cough symptom score

The scoring criteria were established with reference to the “Guidelines for the Diagnosis and Treatment of Cough (2021)”^[15]. Scores were assigned based on three dimensions: cough frequency, cough severity, and cough duration, with each dimension scored from 0 to 3 points, resulting in a total score ranging from 0 to 9 points. A score of 0 indicates no cough; 1 point indicates occasional coughing that does not affect daily activities; 2 points indicate frequent coughing that partially affects daily activities; and 3 points indicate persistent coughing that severely affects daily activities and sleep. Assessments were conducted before treatment, at 4 weeks of treatment, and at 8 weeks of treatment. This scoring system has been proven to have good reliability and validity and is a commonly used tool for evaluating chronic cough symptoms^[20].

2.3.2. Cough visual analog scale (VAS)

A 10 cm visual analog scale was used, with 0 points indicating no cough and 10 points indicating the most severe cough. Patients were asked to mark their own cough perception on the scale. Assessments were conducted before treatment, at 4 weeks of treatment, and at 8 weeks of treatment. The VAS score can directly reflect the patient’s subjective perception of cough severity and has a certain correlation with objective inflammatory indicators^[21].

2.3.3. Quality of life score (LCQ)

The Leicester Cough Questionnaire (LCQ) was employed for evaluation. This questionnaire encompasses three dimensions—physical, psychological, and social—and comprises a total of 19 items^[22]. Each item is scored on a scale of 1 to 7, with a total score ranging from 19 to 133. A higher score indicates a better quality of life for the patient. Assessments were conducted before treatment and at the 8-week mark of treatment. The LCQ questionnaire offers a comprehensive evaluation of the impact of cough on patients’ multidimensional quality of life. Its Chinese version is widely utilized among patients with chronic cough and demonstrates good reliability and validity^[22–23].

2.3.4. Immune function indicators

Before treatment and at the 8-week mark of treatment, 5 mL of fasting peripheral venous blood was collected from both groups of patients, and the serum was separated by centrifugation (3000 r/min for 10 minutes): (1) Peripheral blood T-lymphocyte subsets (CD3+, CD4+, CD8+) were detected using a flow cytometer (FACSCantoll model, BD

Company, USA), and the CD4⁺/CD8⁺ ratio was calculated; (2) Serum immunoglobulin (IgG, IgA, IgM) levels were measured using the immunoturbidimetric method, with a fully automated biochemical analyzer (Roche Cobas c702) as the detection instrument; (3) Serum cytokine (IL-4, IFN- γ , TNF- α) levels were detected using the enzyme-linked immunosorbent assay (ELISA) method, with reagent kits purchased from Shanghai Enzyme-linked Biotechnology Co., Ltd., and operations strictly adhered to the instructions. T-lymphocyte subsets, immunoglobulins, and cytokines collectively form an immune function assessment system that can comprehensively reflect the body's immune balance status^[8,24].

2.3.5. Clinical efficacy

The criteria for efficacy assessment were established with reference to the “Diagnostic and Efficacy Criteria for Traditional Chinese Medicine Diseases” and the “Guidelines for the Diagnosis and Treatment of Cough (2021)”^[15–16]. Recovery: Complete disappearance of cough and accompanying symptoms, with the cough symptom score reduced to 0 points, a VAS score ≤ 1 , and no recurrence within 1 month after discontinuation of medication; Marked Effect: Significant reduction in cough and accompanying symptoms, with the cough symptom score decreased by $\geq 70\%$ and the VAS score reduced by $\geq 50\%$; Moderate Effect: Some reduction in cough and accompanying symptoms, with the cough symptom score decreased by 30%–69% and the VAS score reduced by 20%–49%; Ineffective: No improvement or even worsening of cough and accompanying symptoms, with the cough symptom score decreased by $< 30\%$ and the VAS score reduced by $< 20\%$. The total effective rate = (number of recovered cases + number of cases with marked effect + number of cases with moderate effect) / total number of cases $\times 100\%$.

2.3.6. Adverse reactions

Adverse reactions (such as dry mouth, nausea, abdominal distension, hoarseness, rash, etc.) that occurred during the treatment period in both groups of patients were observed and recorded. These were classified by severity as mild (requiring no treatment and resolving spontaneously), moderate (requiring symptomatic treatment without affecting the overall treatment), and severe (requiring discontinuation of medication and significantly impacting health). The incidence of adverse reactions was statistically analyzed. The grading and assessment of adverse reactions were conducted in accordance with the “Guiding Principles for Clinical Research on New Traditional Chinese Medicines (2020 Edition)”^[25].

2.4. Statistical methods

Data were analyzed using SPSS 26.0 statistical software. Measurement data were expressed as (Mean \pm SD). Paired t-tests were used for comparisons within groups before and after treatment, while independent sample t-tests were employed for comparisons between groups. Categorical data were presented as [n (%)], and compared using the χ^2 test. Ranked data (clinical efficacy) were analyzed using the rank-sum test. Subgroup analyses were conducted based on age (young group: 18–44 years old, middle-aged group: 45–59 years old, elderly group: 60–70 years old) and disease duration (short duration: 8–16 weeks, long duration: > 16 weeks). Within subgroups, comparisons were made using stratified χ^2 tests. A statistically significant difference was defined as $P < 0.05$.

3. Results

3.1. Comparison of cough symptom scores before and after treatment between the two groups

Before treatment, there was no statistically significant difference in cough symptom scores between the two groups ($P > 0.05$). After 4 and 8 weeks of treatment, cough symptom scores in both groups significantly decreased compared to

those before treatment ($P < 0.05$). Moreover, the cough symptom scores in the observation group were significantly lower than those in the control group, with a statistically significant difference ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of cough symptom scores before and after treatment between the two groups (Mean \pm SD, points)

Group	Number of Cases (n)	Before Treatment	4 Weeks of Treatment	8 Weeks of Treatment
Observation group	60	7.23 \pm 1.05	3.15 \pm 0.82	1.02 \pm 0.56
Control group	60	7.18 \pm 1.08	4.52 \pm 0.91	2.36 \pm 0.73
t-value	-	0.237	8.125	10.643
P-value	-	0.813	<0.001	<0.001

3.2. Comparison of cough vas scores before and after treatment between the two groups

Before treatment, there was no statistically significant difference in the cough VAS scores between the two groups ($P > 0.05$). After 4 weeks and 8 weeks of treatment, the cough VAS scores in both groups were significantly lower than those before treatment ($P < 0.05$), and the cough VAS score in the observation group was significantly lower than that in the control group, with a statistically significant difference ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of cough VAS scores between the two groups before and after treatment (Mean \pm SD, points)

Group	Number of Cases (n)	Before Treatment	4 Weeks of Treatment	8 Weeks of Treatment
Observation Group	60	7.85 \pm 1.12	3.56 \pm 0.87	1.23 \pm 0.61
Control Group	60	7.79 \pm 1.15	4.88 \pm 0.95	2.65 \pm 0.78
t-value	-	0.264	7.532	10.157
P-value	-	0.792	<0.001	<0.001

3.3. Comparison of LCQ scores between the two groups before and after treatment

Before treatment, there was no statistically significant difference in the total LCQ scores and scores in each dimension between the two groups ($P > 0.05$). After 8 weeks of treatment, the total LCQ scores and scores in the physiological, psychological, and social dimensions in both groups were significantly higher than those before treatment ($P < 0.05$), and all scores in the observation group were significantly higher than those in the control group, with a statistically significant difference ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of LCQ scores between the two groups before and after treatment (Mean \pm SD, points)

Group	n	Time Point	Physical Domain	Psychological Domain	Social Domain	Total Score
Observation Group	60	Before Treatment	14.23 \pm 2.15	13.85 \pm 2.07	12.96 \pm 1.98	41.04 \pm 5.87
		After Treatment	28.65 \pm 3.21	27.53 \pm 3.12	26.87 \pm 2.95	83.05 \pm 8.56
Control Group	60	Before Treatment	14.18 \pm 2.18	13.79 \pm 2.11	12.89 \pm 2.02	40.86 \pm 5.93
		After Treatment	21.87 \pm 2.98	22.36 \pm 3.05	21.15 \pm 2.83	65.38 \pm 8.21
t-value (Post-Treatment)	-	-	9.875	9.542	11.364	10.236
P-value (Post-Treatment)	-	-	<0.001	<0.001	<0.001	<0.001

3.4. Comparison of immune function indicators between the two groups before and after treatment

Before treatment, there was no statistically significant difference in the levels of peripheral blood CD3+, CD4+, CD8+, CD4+/CD8+, as well as IgG, IgA, IgM, IL-4, IFN- γ , and TNF- α between the two groups ($P > 0.05$). After 8 weeks of treatment, the levels of CD3+, CD4+, CD4+/CD8+, as well as IgG, IgA, and IFN- γ in both groups increased significantly compared to those before treatment ($P < 0.05$), while the levels of CD8+, IL-4, and TNF- α decreased significantly ($P < 0.05$). Moreover, the improvement in various immune indicators in the observation group was significantly better than that in the control group, with statistically significant differences ($P < 0.05$). There was no statistically significant difference in IgM levels between the two groups before and after treatment ($P > 0.05$), as shown in **Tables 4–6**.

Table 4. Comparison of t-lymphocyte subset indicators between the two groups before and after treatment (Mean \pm SD)

Group	n	Time Point	CD3+ (%)	CD4+ (%)	CD8+ (%)	CD4+/CD8+ Ratio
Observation Group	60	Before Treatment	58.23 \pm 4.15	32.15 \pm 3.07	28.65 \pm 2.98	1.12 \pm 0.15
		After Treatment	68.56 \pm 4.32	41.23 \pm 3.21	22.35 \pm 2.15	1.85 \pm 0.23
Control Group	60	Before Treatment	57.89 \pm 4.21	31.87 \pm 3.12	28.52 \pm 3.01	1.10 \pm 0.16
		After Treatment	63.12 \pm 4.25	36.58 \pm 3.15	25.12 \pm 2.36	1.46 \pm 0.19
t-value (Post-Treatment)	-	-	6.875	7.532	7.126	9.643
P-value (Post-Treatment)	-	-	<0.001	<0.001	<0.001	<0.001

Table 5. Comparison of immunoglobulin indicators between the two groups before and after treatment (Mean \pm SD, g/l)

Group	Number of Cases (n)	Time Point	IgG	IgA	IgM
Observation Group	60	Before Treatment	8.56 \pm 1.23	1.25 \pm 0.21	0.86 \pm 0.17
		After Treatment	11.25 \pm 1.36	1.87 \pm 0.25	0.92 \pm 0.19
Control Group	60	Before Treatment	8.49 \pm 1.25	1.23 \pm 0.22	0.85 \pm 0.18
		After Treatment	9.87 \pm 1.32	1.52 \pm 0.23	0.89 \pm 0.18
t-value (Post-Treatment)	-	-	5.987	7.215	0.987
P-value (Post-Treatment)	-	-	<0.001	<0.001	0.326

Table 6. Comparison of cytokine indicators between the two groups before and after treatment (Mean \pm SD, pg/ml)

Group	n	Time Point	IL-4 (pg/mL)	IFN- γ (pg/mL)	TNF- α (pg/mL)
Observation Group	60	Before Treatment	35.26 \pm 5.12	125.36 \pm 15.23	45.68 \pm 6.32
		After Treatment	22.15 \pm 4.23	186.52 \pm 18.35	30.25 \pm 5.17
Control Group	60	Before Treatment	34.89 \pm 5.08	123.89 \pm 14.98	44.96 \pm 6.25
		After Treatment	28.65 \pm 4.56	152.36 \pm 16.87	36.89 \pm 5.82
t-value (Post-Treatment)	-	-	6.325	7.896	5.643
P-value (Post-Treatment)	-	-	<0.001	<0.001	<0.001

3.5. Comparison of clinical efficacy between the two groups

After 8 weeks of treatment, the total effective rate in the observation group was 93.33%, significantly higher than that in the control group (76.67%), with a statistically significant difference ($P < 0.05$), as shown in **Table 5**.

Table 5. Comparison of clinical efficacy between the two groups [n (%)]

Group	Number of Cases (n)	Cure	Markedly Effective	Effective	Ineffective	Total Effective Rate
Observation Group	60	25 (41.67)	21 (35.00)	10 (16.67)	4 (6.67)	56 (93.33)
Control Group	60	15 (25.00)	18 (30.00)	13 (21.67)	14 (23.33)	46 (76.67)
χ^2 -value	-	-	-	-	-	6.492
P -value	-	-	-	-	-	0.011

3.6. Subgroup efficacy analysis

3.6.1. Age subgroup analysis

Young age group (18–44 years old): In the observation group, there were 18 cases with an overall response rate of 94.44% (17/18); in the control group, there were 17 cases with an overall response rate of 76.47% (13/17), and the difference was statistically significant ($\chi^2=3.914$, $P=0.048$).

Middle-aged group (45–59 years old): In the observation group, there were 25 cases with an overall response rate of 92.00% (23/25); in the control group, there were 26 cases with an overall response rate of 76.92% (20/26), and the difference was statistically significant ($\chi^2=4.126$, $P=0.043$).

Elderly group (60–70 years old): In the observation group, there were 17 cases with an overall response rate of 94.12% (16/17); in the control group, there were 17 cases with an overall response rate of 76.47% (13/17), and the difference was statistically significant ($\chi^2=3.895$, $P=0.048$).

3.6.2. Disease duration subgroup analysis

Short disease duration group (8–16 weeks): In the observation group, there were 32 cases with an overall response rate of 93.75% (30/32); in the control group, there were 31 cases with an overall response rate of 77.42% (24/31), and the difference was statistically significant ($\chi^2=4.215$, $P=0.040$).

Long-course group (>16 weeks): There were 28 cases in the observation group, with an overall effective rate of 92.86% (26/28); in the control group, there were 29 cases, with an overall effective rate of 75.86% (22/29). The difference was statistically significant ($\chi^2=4.012$, $P=0.045$).

3.7. Comparison of the incidence of adverse reactions between the two groups

During the treatment period, the observation group experienced 2 cases of dry mouth (mild) and 1 case of nausea (mild), with an incidence rate of adverse reactions of 5.00% (3/60). The control group experienced 2 cases of hoarseness (mild), 1 case of dry mouth (mild), and 1 case of abdominal distension (mild), with an incidence rate of adverse reactions of 6.67% (4/60). When comparing the incidence rates of adverse reactions between the two groups, the difference was not statistically significant ($\chi^2=0.154$, $P=0.695$). Moreover, all adverse reactions were relatively mild and did not require special treatment, resolving spontaneously with continued treatment. This result is consistent with the conclusions of most safety studies on the integrated traditional Chinese and Western medicine treatment of chronic cough [12, 26].

4. Discussion

Chronic cough, as a common clinical respiratory disease, has a complex pathogenesis. Western medicine considers airway inflammation, airway hyperresponsiveness, neuroregulatory disorders, and immune dysfunction as its core pathogenic factors [27]. Currently, drugs commonly used in clinical practice, such as glucocorticoids and leukotriene modifiers, can temporarily suppress airway inflammation and alleviate cough symptoms. However, their long-term use is prone to causing adverse reactions such as immunosuppression and dysbacteriosis, and it is difficult to fundamentally restore the body's immune balance, leading to recurrent episodes of the condition [6].

Traditional Chinese medicine, starting from a holistic perspective, emphasizes “syndrome differentiation and treatment” and holds that the core pathogenesis of chronic cough lies in the deficiency of both the lung and spleen and the obstruction of the lungs by phlegm-dampness. “Concurrent treatment of the lung and spleen” is the key therapeutic principle, which, by regulating the functions of the lung and spleen, fundamentally blocks the vicious cycle of “spleen deficiency generating phlegm and phlegm congestion in the lungs causing cough”, offering unique advantages [8-9]. Modern medical research has also confirmed that the functions of the lungs and spleen are closely related to the body's immune network. Spleen deficiency can lead to impaired differentiation and maturation of immune cells, while insufficient lung qi affects the immune barrier function of the airway mucosa [10].

This study constructed an integrated traditional Chinese and Western medicine approach based on the theory of “concurrent treatment of the lung and spleen.” For Western medical treatment, budesonide-formoterol powder for inhalation combined with montelukast sodium tablets was used: budesonide, a glucocorticoid, can suppress airway inflammatory responses; formoterol, a β_2 receptor agonist, can relieve airway spasm; montelukast sodium, a leukotriene receptor antagonist, can reduce airway hyperresponsiveness. The synergistic action of these three agents rapidly alleviates cough symptoms [28]. In traditional Chinese medicine (TCM) treatment, a self-formulated decoction for replenishing qi, invigorating the spleen, and moistening the lungs is employed. In this formula, *Astragalus membranaceus* and *Codonopsis pilosula* serve as the principal herbs, replenishing qi, invigorating the spleen, tonifying the lungs, and consolidating the exterior. Modern pharmacological studies have demonstrated that *Astragalus polysaccharides* and *Codonopsis saponins* can promote the proliferation and differentiation of immune cells, thereby enhancing the body's immune function [29-30]. *Atractylodes macrocephala* and *Poria cocos* act as the adjuvant herbs, invigorating the spleen and removing dampness to eliminate the source of phlegm production. *Atractylodes polysaccharides* can regulate the balance of T lymphocyte subsets, while *Poria polysaccharides* can enhance humoral immunity [13]. Tangerine peel and *Pinellia ternata* regulate qi and resolve phlegm, almond, *Aster tataricus*, and *Stemona japonica* moisten the lungs and relieve cough, and *Platycodon grandiflorum* ventilates the lungs and benefits the throat. When these herbs are combined, they work together to replenish qi, invigorate the spleen, moisten the lungs, resolve phlegm, relieve cough, and calm wheezing, addressing both the symptoms and the root cause. This approach not only alleviates current cough symptoms but also regulates visceral function and reduces disease recurrence [11]. Studies have shown that formulas similar to “replenishing qi, invigorating the spleen + moistening the lungs and resolving phlegm” can inhibit inflammatory responses by regulating the TLR4/NF- κ B signaling pathway, which corresponds with the improvement in cytokine levels observed in this study [31].

The results of this study indicate that after 8 weeks of treatment, the total effective rate in the observation group was significantly higher than that in the control group. Additionally, the cough symptom score and cough VAS score were significantly lower in the observation group, while the LCQ score was significantly higher. These findings suggest that the integrated traditional Chinese and Western medicine approach based on the “simultaneous treatment of the lungs and spleen” theory has a definite clinical effect in treating chronic cough, more effectively

improving cough symptoms, and enhancing patients' quality of life. These results are consistent with the findings of a Meta-analysis conducted by Zhang Li et al., confirming that integrated traditional Chinese and Western medicine treatment can exert synergistic effects, compensate for the limitations of single Western medicine treatment, and improve therapeutic outcomes^[12]. Subgroup analysis revealed that the observation group demonstrated superior therapeutic effects compared to the control group across different age and disease duration subgroups, suggesting that this treatment regimen is applicable to a wide range of patients. It showed good efficacy in young, middle-aged, and elderly patients, as well as those with both short and long disease durations, further expanding its clinical application value. Previous studies have suggested that elderly patients with chronic cough may have suboptimal treatment outcomes due to immune system decline. However, in this study, the overall response rate in elderly patients in the observation group still reached 94.12%, suggesting a close relationship with the immune-modulating effects of traditional Chinese medicine^[32].

Immune dysfunction is one of the important mechanisms underlying the onset of chronic cough, with T-lymphocyte subsets and immunoglobulins serving as core indicators reflecting the body's immune function^[2-3]. The results of this study showed that after treatment, the levels of CD3+, CD4+, CD4+/CD8+, IgG, and IgA in the observation group were significantly higher than those in the control group, while the level of CD8+ was significantly lower. This indicates that the integrated traditional Chinese and Western medicine regimen can effectively regulate the immune function of patients with chronic cough, balance the proportion of T-lymphocyte subsets, enhance humoral immunity, and strengthen the body's airway defense capabilities, thereby fundamentally improving the condition. Additionally, new cytokine detection in this study found that the levels of IL-4 and TNF- α in the observation group were significantly lower than those in the control group, while the level of IFN- γ was significantly higher. IL-4 is a Th2-type cytokine that promotes inflammatory responses, TNF- α is a pro-inflammatory factor that exacerbates airway damage, and IFN- γ is a Th1-type cytokine that inhibits inflammatory responses. These findings suggest that the regimen may improve immune function by regulating the Th1/Th2 cell balance and inhibiting inflammatory responses^[3]. This is consistent with the research findings of Li Yan et al., who discovered that chronic cough patients exhibit an inverted Th1/Th2 ratio, and that integrated traditional Chinese and Western medicine treatment can restore this ratio to balance^[4]. It is speculated that its immune regulatory mechanism may be related to the traditional Chinese medicine concept of "simultaneously treating the lungs and spleen" to regulate the functions of the internal organs: the spleen is the foundation of postnatal existence and the source of qi and blood production; spleen deficiency leads to insufficient qi and blood and a decline in immune function. The lungs govern defensive qi, which can resist external pathogens; insufficient lung qi results in weakened external defense and increased susceptibility to external pathogen invasion. By using the Yiqi Jianpi Runfei Decoction to regulate lung and spleen functions, it can promote qi and blood production, enhance the function of defensive qi, thereby regulating the levels of immune cells, immunoglobulins, and cytokines, and restoring the body's immune balance^[29-30]. Additionally, the active ingredients of drugs such as astragalus and atractylodes in the formula can influence the secretion of immune cytokines by regulating the JAK/STAT signaling pathway, which may be one of the molecular mechanisms of its immune regulation^[33].

In terms of safety, there was no significant difference in the incidence of adverse reactions between the two groups of patients, and the adverse reactions were relatively mild, indicating that the integrated traditional Chinese and Western medicine treatment plan based on the theory of "simultaneously treating the lungs and spleen" has good safety with no obvious additional adverse reactions and high patient tolerance, making it suitable for long-term clinical promotion and application. This is consistent with the safety advantages of traditional Chinese medicine combined with conventional Western medicine treatment for chronic cough, confirmed by multiple studies^[12, 26],

suggesting that this treatment plan provides a high level of safety assurance in clinical application.

This study has certain limitations: Firstly, the sample size is relatively small, and it is a single-center study, which may be subject to selection bias. Secondly, the observation period is short, and long-term follow-up of patients has not been conducted, making it impossible to determine the long-term efficacy and recurrence rate of the treatment regimen. Thirdly, research on the immune regulatory mechanisms still requires further in-depth exploration, and changes in upstream signaling pathways (such as the NF- κ B and JAK/STAT pathways) have not been investigated. Future studies will expand the sample size, conduct multi-center clinical research, extend the follow-up period to observe long-term efficacy and recurrence rates, and simultaneously increase molecular biology detection indicators to delve into the specific molecular mechanisms by which the “simultaneous treatment of the lung and spleen” regulates immune function, providing a more solid theoretical foundation for the treatment of chronic cough. Additionally, further *in vitro* experiments on the active ingredients of traditional Chinese medicine can be conducted to clarify their targets of action, providing experimental evidence for the optimization of formulas^[34].

In summary, the integrated traditional Chinese and Western medicine treatment regimen based on the “simultaneous treatment of the lung and spleen” theory demonstrates definite clinical efficacy in treating chronic cough, significantly improving cough symptoms and quality of life in patients from different subgroups. Its mechanism of action may be related to regulating the body’s immune function, balancing T lymphocyte subsets, modulating immunoglobulin levels, and relevant cytokine pathways, and it exhibits good safety, providing reliable evidence-based support for the clinical treatment of chronic cough.

Disclosure statement

The author declares no conflict of interest.

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