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ARTICLE

Thymosin α1 Combined With 2HRZE/4HR Regimen as a Potential Treatment of Pulmonary Tuberculosis: An Analysis of Immune Function, Pulmonary Function and Inflammatory Response

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Abstract

Aims/Background Immunotherapy plays a critical role in the clinical treatment of tuberculosis, an infectious disease caused by *Mycobacterium tuberculosis*, in which immune damage promotes the occurrence and development of the disease. This study aimed to investigate the efficacy of thymosin α1 combined with the 2HRZE/4HR (2 months of isoniazid, rifampin, pyrazinamide, and ethambutol followed by 4 months of isoniazid and rifampin) in the treatment of pulmonary tuberculosis and its effect on immune function and inflammatory factors.

Methods A retrospective analysis was conducted on 106 pulmonary tuberculosis patients treated between October 2022 and June 2024. The patients were divided into two groups based on their treatment regimens: the control group ($n = 47$) received the 2HRZE/4HR treatment, while the observation group ($n = 59$) received thymosin α1 in addition to the 2HRZE/4HR treatment. All patients underwent a 6-month treatment course. Clinical efficacy was evaluated 6 months after treatment based on clinical symptoms and sputum smear results. The study compared foci resorption rates, cavity closure rates, and changes in pulmonary function indices, immune function indices, and inflammatory factor levels before and after treatment between the two groups. Adverse reactions were also recorded and analyzed.

Results The total effective rate and the rate of foci resorption and cavity closure of the observation group were higher than the control group ($p < 0.05$). After 6 months of treatment, forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC, and peak expiratory flow (PEF) of the observation group were higher compared to the control group ($p < 0.05$). Compared with the control group, the observation group exhibited lower mRNA expression of T-cell immunoglobulin mucin-1 (*TIM-1*) and *TIM-3*; reduced levels of immunoglobulin E (IgE), sputum supernatant, serum interleukin-4 (IL-4) and tumor necrosis factor-alpha (TNF-α); but higher interferon-gamma (IFN-γ) levels ($p < 0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($p > 0.05$).

Conclusion Thymosin α1 combined with the 2HRZE/4HR regimen holds promise as an effective treatment of pulmonary tuberculosis by improving immune function and pulmonary function of patients while attenuating the inflammatory response.

Key words: tuberculosis; thymosin α1; 2HRZE/4HR; clinical efficacy; immune function; inflammatory factors

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Introduction

At present, pulmonary tuberculosis ranks 13th among the leading causes of death in the world, posing a critical threat to the physical and mental health of the affected individuals. Among 30 countries with a high burden of tuberculosis, the estimated number of tuberculosis cases in China ranks third in the world, accounting for 7.4% of global tuberculosis cases (World Health Organization, 2023). With disease progression, advanced cases may present with life-threatening complications potentially involving multiple organ systems, including massive hemoptysis, respiratory failure, and tuberculous meningitis. The 2HRZE/4HR (2 months of isoniazid, rifampin, pyrazinamide, and ethambutol followed by 4 months of isoniazid and rifampin) regimen is the standard first-line treatment for pulmonary tuberculosis, which effectively alleviates clinical symptoms. However, accumulating evidence indicates that while this chemotherapy protocol eradicates *Mycobacterium tuberculosis*, it may also damage normal leukocytes, compromise immune function, and increase susceptibility to microbial infections (Kolloli et al, 2024). Epidemiological data suggest that disease progression is closely associated with host immune status, highlighting the critical role of immune modulation in tuberculosis management (Liu et al, 2024a; Khan et al, 2020). Thymosin α1, a bioactive peptide immunomodulator, exerts its effects through regulating T lymphocyte subsets, promoting T-cell proliferation/differentiation, and restoring T helper 1 cell/T helper 2 cell (Th1/Th2) balance (Chen et al, 2022). Despite its theoretical advantages, the clinical efficacy of thymosin α1 combined with standard chemotherapy remains incompletely understood. Therefore, this study aimed to evaluate the therapeutic effects of thymosin α1 adjuvant therapy combined with the 2HRZE/4HR regimen on pulmonary tuberculosis patients, with a specific focus on improving immune function and inflammatory cytokine profiles. The findings may provide novel insights into optimizing tuberculosis treatment strategies.

Methods

Study Participants

A total of 106 patients with pulmonary tuberculosis treated in the Affiliated Hospital of Shaoxing University were included for retrospective analysis from October 2022 to June 2024 (Fig. 1). The patients were included according to the criteria in the following: (i) diagnosed with pulmonary tuberculosis determined according to diagnostic criteria (Chinese Medical Association, 2019) and chest X-ray results showing active tuberculosis foci; (ii) aged from 18 to 80 years; (iii) having received primary treatment for tuberculosis; and (iv) having completed the treatment. Exclusion criteria of the present study are as follows: (i) patients with critical abnormalities in heart, liver and kidney functions; (ii) patients with histories of drug allergy; (iii) patients with other infectious diseases; (iv) patients with immune system diseases; (v) pregnant or breastfeeding women; (vi) patients with malignant tumors; (vii) patients with chronic inflammatory diseases; (viii) patients with history of anti-tuberculosis treatment; (ix) withdraw from the research for personal reasons; and (x) patients who had received immunostimulants or immunosuppressants that

affect immune function within the last three months prior to enrollment. Patients were divided into two groups based on their treatment regimens (primarily based on the patient's own choice): the control group (n = 47) and the observation group (n = 59). This study has been approved by the Medical Ethics Committee of the Affiliated Hospital of Shaoxing University (Approval No. 2024 (Research)-002-01) and was conducted in strict adherence to the Declaration of Helsinki. Informed consent was obtained from patients in this study.

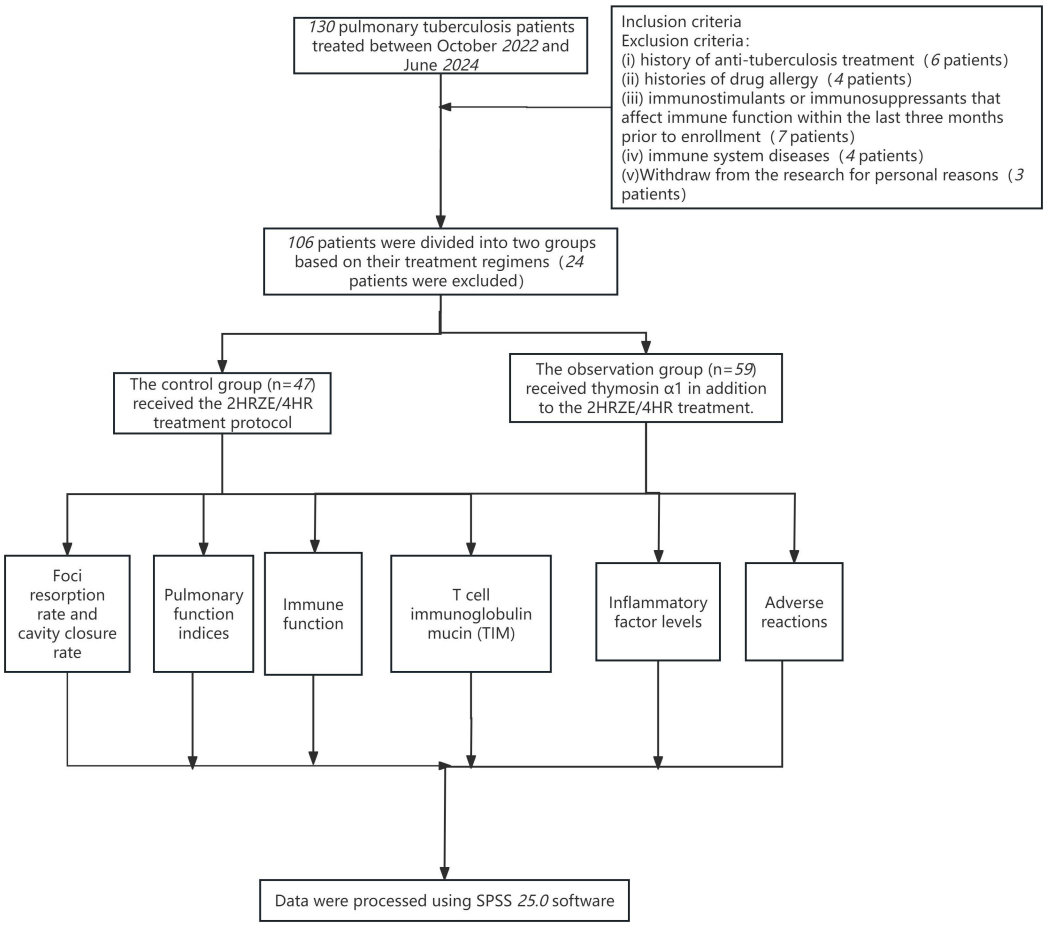

Fig. 1. Flow chart depicting the recruitment of study participants and grouping. 2HRZE/4HR, 2 months of isoniazid, rifampin, pyrazinamide, and ethambutol followed by 4 months of isoniazid and rifampin.

In this retrospective analysis of the therapeutic effects of different treatment methods on pulmonary tuberculosis, pulmonary tuberculosis patients were divided into two groups based on the type of treatment administered. Clinical efficacy was regarded as the main observation index. Based on the literature (He and Zheng, 2021), the effective rate of the 2HRZE/4HR treatment protocol in treating pulmonary tuberculosis was 80%–90%. Sample size calculation formula: $n_c = [\pi_t(1 - \pi_t)/\kappa + \pi_c(1 - \pi_c)](u_{1-\alpha/2} + u_{1-\beta})^2/(\pi_t - \pi_c)^2$. Meanwhile, α was set at 0.05 and β at 0.1, i.e., $u_{1-\alpha/2}$ was 1.96 and $u_{1-\beta}$ was 0.84. π_t was the proportion of the observation group; π_c was the proportion of the control group; κ was the pro-

portion of the number of cases in the two groups. By substituting the proportions of the two groups into the formula, n was calculated as 45. Therefore, the number of patients in each group needs to be greater than 45. Considering that 30% of the patients might be excluded, 65 cases were recruited for each of the two groups.

Intervention

The control group was treated with the 2HRZE/4HR regimen, consisting of isoniazid tablets (National Medicine Permit No. H33021636, Lot.T22F046, Minsheng Pharmaceutical Co., Ltd., Hangzhou, China) 0.3 g/d, p.o.; rifampicin tablets (National Medicine Permit No. H32020147, Lot.23070611, Yuexing Pharmaceutical Co., Ltd., Xinghua, China) 0.45 g/d, p.o.; pyrazinamide tablets (National Medicine Permit No. H21022354, Lot.E0422021, Hongqi Pharmaceutical Co., Ltd., Shenyang, China) 1.5 g/d, p.o.; and ethambutol tablets (National Medicine Permit No. H33021602, Lot.T23N007, Minsheng Pharmaceutical Co., Ltd., Hangzhou, China) 0.75 g/d, p.o. In the event that the sputum smear remained positive 2 months after the intensive treatment, a similar treatment course was extended by 1 month, consolidated with isoniazid, rifampicin (HR). On the basis of the treatment given to the patients in the control group, thymosin α1 (National Medicine Permit No. H20030407, Shuangcheng Pharmaceutical Co., Ltd., Haikou, China) was given to patients in the observation group by subcutaneous injection at 1.6 mg/time, 2 times/week, p.o. All the patients were treated as described for 6 months.

Determination of Clinical Efficacy

According to the Guideline for the Diagnosis and Treatment of Tuberculosis (Chinese Medical Association, 2019), clinical efficacy is divided into several classifications:

(i) Cure: Sputum, cough, fever, chest pain, fatigue and other clinical symptoms resolve completely; sputum smear was negative for bacilli; complete disappearance of lung foci and closure of cavities.

(ii) Markedly effective: Clinical symptoms such as cough, sputum, fever, chest pain, fatigue, etc., resolve moderately; lung foci shrunk $>$50%; cavity shrunk $>$50%.

(iii) Effective: Clinical symptoms such as cough, sputum, fever, chest pain, fatigue, etc., show improvement; foci resorbed by 30%–50%; cavity remains unchanged.

(iv) Ineffective: Clinical symptoms such as cough, fever, chest pain, fatigue, etc., do not show improvement; foci do not shrink or even appear to be enlarged.

The overall effective rate was calculated using the formula below:

Overall effectiveness rate = Cure rate + Markedly effective rate + Effective rate.

Data Collection

Clinical Data Collection

Clinical data such as gender, age, body mass index (BMI), disease duration, previous medical history, history of alcohol consumption and smoking history were collected. Before data collection, researchers were educated about the question-

naire contents, as well as the procedures and precautions of administering the questionnaire. The researchers were also trained in the aspects of filling out the questionnaire. Only the researchers who had passed a training assessment could take up the responsibility of conducting the survey. Before the investigation, all study participants or their families were briefed about the purpose and requirements of the research. The survey was conducted face-to-face. The researchers performed an instant check on the questionnaire after the survey and requested verification if necessary. Missing items were addressed in time. Regular answers were deleted to ensure data accuracy. To reduce human errors attributed to interpersonal variations, the survey was conducted by the same researcher.

Foci Resorption Rate and Cavity Closure Rate

Computed tomography (CT; Lot.01111803130001, SOMATOM Definition AS 128, SIEMENS, Shanghai, China) was used to detect lung foci resorption in patients after 6 months of treatment. A rate of >50% was considered foci resorption.

Pulmonary Function Indices

Lung function indices of the patients were measured using a lung function detector (IQspiro 552242, Fisher Biomedical Incorporated, Venice, FL, USA) before treatment and after 6 months of treatment.

Immune Function

Fasting venous blood was collected from the patients before treatment and after 6 months of treatment. Immunoglobulin levels were measured by means of scattering turbidimetry.

T-Cell Immunoglobulin Mucin (TIM)

Monocytes were isolated by density gradient centrifugation, and peripheral blood lymphocytes were separated using a lymphocyte isolation solution (17-1440, GE Healthcare, Chicago, IL, USA). The purified RNA was then reverse-transcribed to obtain cDNA, and real-time fluorescence quantitative polymerase chain reaction (PCR) was used to detect the levels of T-cell immunoglobulin mucin-1 (*TIM-1*) and *TIM3* mRNA expression. Sequences of primers used in this experiment are as follows: *TIM1*: Reverse Transcription-Forward primer (RT-F) 5′-GAACATAGT CTACTGACGGCCAATAC-3′, Reverse Transcription-Reverse primer (RT-R) 5′-GAACCTCCTTTTTGAAGAAATACTTTTT-3′; *TIM3*: RT-F 5′-AATTGAACTG GGACCTGCAC-3′, RT-R 5′-CTTTCACCTCAGCACCCAGT-3′; *β-actin*: RT-F 5′-AGCCATGTACGTAGCCATCC-3′, RT-R 5′-GACTCCATCACAATGCCAGT-3′.

Inflammatory Factor Levels in Sputum Supernatant and Serum Medicine Permit No. H32020147

Sputum samples were collected from the patients before and after 6 months of treatment. During the collection process, patients were asked to rinse their mouth with water in the morning on an empty stomach. Subsequently, they received intermittent nebulization with 3% saline solution. During this process, patients were en-

couraged to cough out deep sputum. The collected sputum samples were processed using 0.1% dithiothreitol (DTT; 205314, Gentihold Biotechnology Co., Ltd., Beijing, China) and centrifuged (centrifugal speed: 3000 r/minute; time: 10 minutes; centrifuge radius: 10 cm) to obtain the supernatant.

Blood samples were also collected from the patients. Fasting venous blood (3 mL) was collected from each patient. Enzyme-Linked Immunosorbent Assay (ELISA) kits were used to analyze the sputum supernatant and serum samples obtained to detect interleukin-4 (IL-4; EHC006.48, NeoBioscience Technology Co., Ltd., Shenzhen, China), interferon-gamma (IFN-γ; EHC015.96, NeoBioscience Technology Co., Ltd., Shenzhen, China) and tumor necrosis factor-alpha (TNF-α; EHC103a.96, NeoBioscience Technology Co., Ltd., Shenzhen, China).

Adverse Reactions

The incidence of leukopenia, gastrointestinal reactions and liver function impairment in the two groups was analyzed.

Statistical Methods

Data were processed using SPSS 25.0 software (IBM Corporation, Armonk, NY, USA). Categorical data are expressed as frequency and percentage. Chi-square test and Yates's corrected chi-square test were employed to perform comparative analysis of categorical data between groups. Continuous data were tested for normality using the Shapiro-Wilk test. Expressed as mean ± standard deviation, normally distributed data between groups were compared using the independent sample *t*-test, whereas within-group data were compared using paired samples *t*-test. A p-value < 0.05 was considered statistically significant.

Table 1. Comparison of baseline data between the two groups.

Characteristic	Observation group ($n = 59$)	Control group ($n = 47$)	χ^2/t	p
Gender			0.864	0.353
Male	35 (59.32)	32 (68.09)		
Female	24 (40.68)	15 (31.91)		
Age (years)	49.17 ± 5.74	50.04 ± 6.15	0.751	0.454
BMI (kg/m^2)	21.53 ± 2.07	21.39 ± 2.51	0.315	0.754
Duration (years)	0.11 ± 0.03	0.10 ± 0.03	1.705	0.091
History of smoking	21 (35.59)	20 (42.55)	0.534	0.465
History of alcohol consumption	15 (25.42)	11 (23.40)	0.058	0.810
Hypertension	24 (40.68)	16 (34.04)	0.490	0.484
Diabetes mellitus	19 (32.20)	13 (27.66)	0.256	0.613
Hyperlipidemia	14 (23.73)	10 (21.28)	0.090	0.764
Coronary heart disease	8 (13.56)	5 (10.64)	0.207	0.649

Notes: Categorical data are expressed as n (%), whereas quantitative data are expressed as mean ± standard deviation.
Abbreviation: BMI, body mass index.

Results

Comparison of Baseline Data

There was no significant difference in the baseline data between the two groups ($p > 0.05$) (Table 1).

Comparison of Clinical Efficacy

The overall effective rate of the observation group was higher than that of the control group ($p < 0.05$) (Table 2).

Table 2. Comparison of clinical efficacy between the two groups.

Clinical efficacy classification	Observation group ($n = 59$)	Control group ($n = 47$)	χ^2	p
Cure	13 (22.03)	6 (12.77)		
Markedly effective	19 (32.20)	15 (31.91)		
Effective	25 (42.37)	17 (36.17)		
Ineffective	2 (3.39)	9 (19.15)		
Overall effectiveness rate	57 (96.61)	38 (80.85)	5.394	0.020

Notes: Data are expressed as n (%).

Comparison of Foci Resorption Rate and Cavity Closure Rate

The observation group had higher rates of foci resorption and cavity closure than the control group ($p < 0.05$) (Table 3).

Table 3. Comparison of foci resorption rate and cavity closure rate between the two groups.

Parameter	Observation group ($n = 59$)	Control group ($n = 47$)	χ^2	p
Foci resorption rate	54 (91.53)	32 (68.09)	9.390	0.002
Cavity closure rate	55 (93.22)	35 (74.47)	7.178	0.007

Notes: Data are expressed as n (%).

Comparison of Pulmonary Function Indices

Before treatment, the forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC and peak expiratory flow (PEF) remained comparable between the two groups ($p > 0.05$). However, after 6 months of treatment, these pulmonary indices were higher in the observation group than in the control group ($p < 0.05$) (Table 4).

Comparison of Immunoglobulin Levels

Before treatment, there was no significant difference in immunoglobulin G (IgG), immunoglobulin M (IgM), immunoglobulin A (IgA) and immunoglobulin E (IgE) levels between the two groups ($p > 0.05$). Even after 6 months of treatment, the levels of IgG, IgM and IgA of the observation and control groups remained co-

Table 4. Comparison of pulmonary function indices between the two groups.

Group	*n*	FEV1		FVC		FEV1/FVC		PEF (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	59	1.61 ± 0.25	2.43 ± 0.39*	2.38 ± 0.31	3.21 ± 0.28*	68.77 ± 13.69	75.62 ± 9.46*	73.52 ± 5.16	95.36 ± 2.79*
Control group	47	1.63 ± 0.24	2.25 ± 0.27*	2.42 ± 0.36	3.09 ± 0.25*	67.97 ± 9.72	72.61 ± 3.22*	74.01 ± 7.35	86.19 ± 5.34*
t		0.416	2.691	0.614	2.297	0.338	2.086	0.403	11.391
p		0.678	0.008	0.540	0.024	0.736	0.039	0.688	<0.001

Notes: *$p < 0.05$ compared with before treatment in the same group.
Abbreviations: FEV1, forced expiratory volume in one second; FVC, forced vital capacity; PEF, peak expiratory flow.

Table 5. Comparison of immunoglobulin levels between the two groups.

Group	*n*	IgG (μg/L)		IgM (μg/L)		IgA (μg/L)		IgE (IU/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	59	7.47 ± 0.86	7.56 ± 1.13	1.17 ± 0.21	1.19 ± 0.13	1.56 ± 0.29	1.58 ± 0.21	286.35 ± 20.21	151.36 ± 18.74*
Control group	47	7.41 ± 1.15	7.51 ± 0.98	1.19 ± 0.25	1.20 ± 0.17	1.58 ± 0.31	1.61 ± 0.24	283.71 ± 23.68	171.49 ± 12.01
t		0.307	0.240	0.448	0.343	0.342	0.686	0.619	6.390
p		0.759	0.811	0.655	0.732	0.733	0.494	0.537	<0.001

Notes: *$p < 0.05$ compared with before treatment in the same group.
Abbreviations: IgA, immunoglobulin A; IgE, immunoglobulin E; IgG, immunoglobulin G; IgM, immunoglobulin M.

mparable ($p > 0.05$), except for the IgE level, which was significantly lower in the observation group than in the control group ($p < 0.05$) (Table 5).

Comparison of TIM Expression

Before treatment, there was no significant difference in the *TIM1* and *TIM3* mRNA expression between the two groups ($p > 0.05$). After 6 months of treatment, *TIM1* and *TIM3* mRNA expression in the observation group was lower than that in the control group ($p < 0.05$) (Table 6).

Table 6. Comparison of *TIM1* and *TIM3* mRNA expression levels between the two groups.

Group	*n*	*TIM1*		*TIM3*	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	59	2.31 ± 0.45	1.29 ± 0.24*	1.79 ± 0.28	1.16 ± 0.18*
Control group	47	2.25 ± 0.37	1.41 ± 0.28*	1.75 ± 0.25	1.31 ± 0.16*
t		0.737	2.375	0.766	4.475
p		0.463	0.019	0.446	<0.001

Notes: *$p < 0.05$ compared with before treatment in the same group.
Abbreviation: TIM, T-cell immunoglobulin mucin.

Comparison of Inflammatory Factor Levels in Sputum Supernatant

Before treatment, there were no significant differences in the IL-4, IFN-γ and TNF-α levels in the sputum supernatant between the two groups ($p > 0.05$). After 6 months of treatment, the levels of IL-4 and TNF-α in the observation group were lower than those in the control group, and the levels of IFN-γ were higher than those in the control group ($p < 0.05$) (Table 7).

Comparison of Inflammatory Factor Levels in Serum

Before treatment, there were no significant differences in the serum IL-4, IFN-γ, and TNF-α levels between the two groups ($p > 0.05$). After 6 months of treatment, the IFN-γ level of the observation group was higher than that of the control group, and the IL-4 and TNF-α levels were lower than that of the control group ($p < 0.05$) (Table 8).

Adverse Reactions

There was no significant difference in the incidence rate of adverse reactions between the two groups ($p > 0.05$) (Table 9).

Discussion

Pulmonary tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis* in the lungs, characterized by clinical manifestations such as cough, chest pain, and fatigue. Progressive disease can lead to significant pulmonary damage, accelerate nutritional depletion, compromise immune function, and ultimately affect prognosis (Wen et al, 2022). In clinical management, the pri-

Table 7. Comparison of inflammatory factor levels in sputum supernatant between the two groups.

Group	*n*	IL-4 (ng/L)		IFN-γ (ng/L)		TNF-α (ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	59	191.65 ± 17.24	78.31 ± 12.51*	6.19 ± 1.14	20.04 ± 2.46*	537.27 ± 52.78	129.63 ± 24.18*
Control group	47	190.29 ± 13.96	89.54 ± 13.60*	6.25 ± 1.31	17.12 ± 2.08*	534.05 ± 50.64	195.32 ± 25.69*
t		0.438	4.417	0.252	6.494	0.318	13.516
p		0.662	<0.001	0.802	<0.001	0.751	<0.001

Note: *$p < 0.05$ compared with before treatment in the same group.
Abbreviations: IFN-γ, interferon-gamma; IL-4, interleukin-4; TNF-α, tumor necrosis factor-alpha.

Table 8. Comparison of serum inflammatory factor levels between the two groups.

Group	*n*	IFN-γ (ng/L)		IL-4 (ng/L)		TNF-α (ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	59	23.64 ± 5.12	77.52 ± 10.08*	256.58 ± 57.64	102.17 ± 24.82*	682.56 ± 43.27	149.52 ± 25.07*
Control group	47	24.19 ± 5.64	62.47 ± 11.35*	263.97 ± 53.15	137.21 ± 25.17*	687.01 ± 38.74	213.17 ± 26.89*
t		0.525	7.221	0.679	7.176	0.551	12.574
p		0.601	<0.001	0.499	<0.001	0.583	<0.001

Notes: *$p < 0.05$ compared with before treatment in the same group.
Abbreviations: IFN-γ, interferon-gamma; IL-4, interleukin-4; TNF-α, tumor necrosis factor-alpha.

Table 9. Comparison of adverse reaction incidence between the two groups.

Adverse reaction	Observation group (*n* = 59)	Control group (*n* = 47)	χ^2	*p*
Leukopenia	0 (0.00)	1 (2.13)		
Gastrointestinal reactions	1 (1.69)	1 (2.13)		
Liver function impairment	0 (0.00)	1 (2.13)		
Overall incidence rate	1 (1.69)	3 (6.38)	0.556	0.456

Notes: Data are expressed as *n* (%).

mary goal is to achieve a negative sputum smear. Surgical interventions are inherently invasive and their outcomes are uncertain in most cases, thereby positioning conventional anti-tuberculosis chemotherapy as the first-line approach (Kumar et al, 2024). The 2HRZE/4HR regimen is a standard treatment for tuberculosis, but emerging drug resistance and adverse effects have led to compromised therapeutic efficacy and patient compliance (He and Zheng, 2021). A recent study indicates that adjuvant immunotherapy may enhance treatment outcomes by improving host immune responses (Guo et al, 2021). Thymosin α1, a polypeptide extracted from neonatal calf thymus, exerts its immunomodulatory effects by stimulating differentiation of bone marrow-derived stem cells into functional T lymphocytes to achieve restoration of normal protective immune responses and elimination of persistent/dormant mycobacteria mediated by anti-tuberculosis drugs (Tao et al, 2023; Lan et al, 2020). The present study demonstrated that the combined thymosin α1 and 2HRZE/4HR regimen significantly improved overall treatment efficacy rate, foci resorption rate, and cavity closure rate compared to standard therapy alone. This improvement may be attributed to thymosin α1's ability to induce T lymphocyte proliferation/differentiation, maintain $CD4^+/CD8^+$ T-cell balance, and enhance mycobacterial growth inhibition (Liu et al, 2024b). Additionally, post-treatment pulmonary function parameters, including FEV1, FVC, FEV1/FVC ratio, and PEF were significantly higher in patients receiving thymosin α1 in addition to the standard 2HRZE/4HR treatment, suggesting that adjuvant thymosin α1 therapy reduces pulmonary tissue damage through enhanced mycobacterial clearance.

At present, it is believed that *Mycobacterium tuberculosis* infection triggers immunological disorders, with host immune responses serving as the pathological foundation for disease development. Dynamic alterations in lymphocyte and mononuclear macrophage populations play critical roles in disease progression (Vilvamani et al, 2024). The 2HRZE/4HR chemotherapy regimen remains the cornerstone of tuberculosis management, yet accumulating evidence demonstrates that while despite an effective mycobacterial eradication function, these drugs may deplete normal leukocytes, compromise immune function, and increase susceptibility to secondary microbial infections, thereby adversely affecting patient outcomes (Micheni et al, 2021; Combrink et al, 2020). *TIM1* and *TIM3* are two major members of the *TIM* gene family discovered in recent years, which are mainly expressed on the surface of immune cells. Both *TIM1* and *TIM3* modulate Th1 and Th2 cell-mediated immune responses. *TIM1* is mainly expressed on the surface of Th2 cells and plays an important role in regulating the proliferation, differentiation and secretion of cytokines of Th2 cells, while *TIM3* molecules are selectively expressed on the surface of activated Th1 cells but not on the surface of Th2 cells. After binding with *TIM3* ligand, it can inhibit the Th1 type immune response and play a negative immunomodulatory role (Kang et al, 2020). It has been reported that thymosin α1-assisted treatment for recurrent pulmonary tuberculosis combined with diabetes can effectively increase the conversion rate of sputum *Mycobacterium tuberculosis* culture to negative and regulate T lymphocyte subsets, but the treatment's impact on *TIM1* and *TIM3* expression remains poorly understood. Therefore, this study conducted relevant analyses and found that the IgE levels and mRNA ex-

pression of *TIM1* and *TIM3* in the observation group were lower than those in the control group after treatment, indicating that the combination of thymosin α1 and 2HRZE/4HR regimen for treating pulmonary tuberculosis can improve immune function. This immunomodulatory effect likely stems from thymosin α1's ability to promote thymocyte maturation, enhance Th1 differentiation, and stimulate cytokine production, thereby restoring functional T lymphocyte activity (Wu et al, 2022; Chen et al, 2024). Analysis of sputum supernatant and serum inflammatory markers showed that combination therapy reduced IL-4 and TNF-α levels while increasing IFN-γ expression. These changes highlight that thymosin α1 enhances cytotoxic and phagocytic potentials of natural killer cells and macrophages, respectively, while augmenting superoxide dismutase activity to mitigate oxidative damage and inflammation (Ronghua and Zhiyong, 2024; Nevo et al, 2023). Notably, the thymosin α1 adjuvant therapy did not contribute to an increased incidence rate of treatment-related adverse events, confirming its excellent safety profile in clinical practice.

The present study was constrained by several shortcomings, such as: (i) retrospective single-center design, which raises the risk for selection and recall bias; (ii) small sample size; (iii) missing data; and (iv) challenges in controlling the timeliness and integrity of data. Therefore, a multicenter study involving larger samples is warranted to confirm the conclusion of this study in the future.

Conclusion

In conclusion, the present study demonstrated that thymosin α1 combined with 2HRZE/4HR regimen holds promise as a potentially effective treatment approach for pulmonary tuberculosis, marked by its ability in improving the cellular immune function and pulmonary function of patients, and attenuating the inflammatory response of the body. Nevertheless, more investigations should be conducted to corroborate the clinical efficacy of this regimen for the treatment of pulmonary tuberculosis.

Key Points

- Thymosin α1 combined with 2HRZE/4HR regimen provides a more effective avenue for treating pulmonary tuberculosis than the standard 2HRZE/4HR treatment.
- Thymosin α1 combined with 2HRZE/4HR regimen can improve the cellular immune function of patients with pulmonary tuberculosis.
- Thymosin α1 combined with 2HRZE/4HR regimen can improve the pulmonary function of patients with pulmonary tuberculosis.
- Thymosin α1 combined with 2HRZE/4HR regimen can mitigate the inflammatory response in patients with pulmonary tuberculosis.

Availability of Data and Materials

All data included in this study are available from the corresponding author upon reasonable request.

Author Contributions

GFW and XLS designed the research study and wrote the first draft. GFW and XLS performed the research. GFW and XLS analyzed the data. Both authors contributed to the important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study has been approved by the Medical Ethics Committee of the Affiliated Hospital of Shaoxing University (Approval No. 2024 (Research)-002-01) and was conducted in strict adherence to the Declaration of Helsinki. Informed consent was obtained from patients in this study.

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Conflict of Interest

The authors declare no conflict of interest.

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