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Coronavirus Pandemic

Comparative efficacy of Lianhua Qingwen capsules combined with standard care versus standard care alone in patients with mild to moderate COVID-19

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Abstract

Introduction: The COVID-19 pandemic has prompted a search for effective treatments. This study evaluated the efficacy and safety of Lianhua Qingwen capsules combined with standard care for treating patients with mild to moderate COVID-19.

Methodology: A retrospective cohort study was conducted in a tertiary hospital in China between 1 March 2023 and 31 December 2023. The medical records of 284 patients with mild to moderate COVID-19 were analyzed; 142 patients who received Lianhua Qingwen capsules plus standard care were compared with 142 matched controls who received standard care alone. Propensity score matching was used to minimize selection bias. The primary outcomes included time to symptom improvement, time to viral clearance, 14-day clinical recovery rate, improvement in chest computed tomography (CT) findings, and quality of life scores. Secondary outcomes included changes in inflammatory markers, immune function improvement, and adverse event rates.

Results: The Lianhua Qingwen group showed a significantly shorter time to symptom improvement (hazard ratio [HR] 1.43, 95% confidence interval [CI] 1.21–1.69, $p < 0.001$), faster viral clearance (HR 1.52, 95% CI: 1.28–1.80, $p < 0.001$), higher 14-day clinical recovery rate (91.5% vs 82.4%, $p = 0.024$) and more pronounced chest CT improvements (78.9% vs 64.8%, $p = 0.009$). Quality of life scores, inflammatory markers, and immune function improved more in the treatment group. Adverse event rates were similar (12.7% vs 13.4%, $p = 0.856$).

Conclusions: Lianhua Qingwen capsules, when combined with standard care, demonstrated superior efficacy compared with standard care alone in treating mild to moderate COVID-19, with a favorable safety profile. These findings suggest that Lianhua Qingwen capsules could be a valuable adjunct therapy for COVID-19 management.

Key words: COVID-19; Lianhua Qingwen capsules; traditional Chinese medicine; retrospective cohort study; efficacy; safety.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has presented unprecedented challenges to global public health systems and economies [1]. As of August 2024, the virus has infected millions of people worldwide, causing significant morbidity and mortality. Although vaccination efforts have made substantial progress in controlling the spread of the virus, the emergence of new variants and the need for effective treatments for those who do become infected remain critical concerns [2].

The clinical spectrum of COVID-19 ranges from asymptomatic or mild illness to severe pneumonia with acute respiratory distress syndrome and multi-organ failure [3]. Mild to moderate cases, which constitute the majority of infections, are characterised by symptoms such as fever, cough, fatigue**,** and loss of taste or smell. Although these cases generally have a good prognosis, effective treatments are still needed to alleviate symptoms, prevent progression to severe disease**,** and reduce viral shedding to limit transmission.

Standard care for mild to moderate COVID-19 typically includes supportive measures, such as rest, hydration, antipyretics**,** and close monitoring for disease progression. Antiviral medications, such as remdesivir, have shown some efficacy in shortening the duration of illness in hospitalised patients [4]. However, the search for additional effective and safe treatments, particularly for outpatient management of mild to moderate cases, remains an active area of research. Antiviral drugs (such as remdesivir) have shown effects in shortening the course of disease in hospitalised patients, but their application in outpatient treatment is limited. For example, remdesivir requires intravenous injection, which limits its use in outpatient settings, and its efficacy in patients with mild to moderate COVID-19 has not been fully demonstrated [5]. In addition, some other drugs (such as hydroxychloroquine and lopinavir/ritonavir) have also failed to show significant clinical benefits in the treatment of COVID-19 [6]. For example, hydroxychloroquine has failed to shorten the course of disease significantly or reduce hospitalisation

rates in multiple studies and may cause serious adverse reactions, such as arrhythmia [7]. Lopinavir/ritonavir, despite showing certain antiviral activity in vitro experiments, has failed to improve clinical outcomes in patients significantly in clinical trials and may cause gastrointestinal adverse reactions and drug interactions [8].

Traditional Chinese medicine (TCM) has a long history of use in treating respiratory diseases and has been extensively employed in China as part of the integrated approach to managing COVID-19 [9]. Lianhua Qingwen capsules, a patented Chinese herbal formula, have gained particular attention due to their potential antiviral and immunomodulatory effects. The formula consists of 13 herbs, including *Forsythia suspensa*, *Lonicera japonica*, *Ephedra sinica***,** and *Glycyrrhiza uralensis* [10]. The drug was developed based on the TCM theory of 'clearing pestilence and detoxifying and relieving lung heat'. It has a wide range of pharmacological effects, including antiviral, antibacterial, anti-inflammatory, antipyretic, antitussive**,** and immune-regulating properties [11]. The mechanism of action of Lianhua Qingwen capsules mainly includes the following aspects: first, Lianhua Qingwen capsules can inhibit the binding of the S protein of SARS-CoV-2 to the ACE2 receptor of host cells, thereby preventing the virus from invading cells [12]. Its main components, such as cynarin, hesperidin**,** and glycyrrhizic acid, can bind to the ACE2 receptor and inhibit viral adsorption and membrane penetration [12]. Second, Lianhua Qingwen capsules can inhibit the M protein of the virus, thereby preventing viral replication and assembly within cells [12]. In addition, it can alter the morphology of viral particles and reduce the amount of virus in the cell membrane and cytoplasm [13]. Lianhua Qingwen capsules can enhance the host's immune response through multiple pathways. For example, its components can inhibit cytokine storms induced by viruses and reduce the overexpression of pro-inflammatory cytokines, such as tumour necrosis factor and interleukin-6 [12]. Moreover, it can also enhance the body's antiviral ability by upregulating the interferon signalling pathway [12]. Lianhua Qingwen capsules have shown significant efficacy in relieving common symptoms, such as fever, cough**,** and fatigue, and their mechanism of action may be related to their anti-inflammatory and immune-regulating functions [11].

Previous studies have suggested that Lianhua Qingwen capsules may have beneficial effects in treating influenza and other respiratory viral infections [14,15]. Lianhua Qingwen capsules were approved for clinical treatment during the 2003 SARS outbreak and the 2009 H1N1 influenza pandemic, and it has demonstrated good antiviral effects [12]. In vitro studies have demonstrated that Lianhua Qingwen can inhibit SARS-CoV-2 replication and reduce pro-inflammatory cytokine production in infected cells [16]. Furthermore, observational studies and small-scale clinical trials have reported positive outcomes in patients with COVID-19 treated with Lianhua Qingwen as part of an integrated treatment approach [17]. During the COVID-19 pandemic, Lianhua Qingwen capsules were included in the 'Diagnosis and Treatment Protocol for COVID-19' released by the National Health Commission of China and were widely used in the treatment of patients with mild and common types of the disease [12]. Multiple clinical studies have shown that Lianhua Qingwen capsules can significantly shorten the time to symptom relief, increase the clinical cure rate, improve chest computed tomography (CT) imaging manifestations**,** and reduce the levels of inflammatory markers [18].

Despite these promising findings, there is a need for large-scale, rigorous clinical trials to evaluate the efficacy and safety of Lianhua Qingwen capsules in treating COVID-19. Such studies are crucial to provide evidence-based guidance for the potential incorporation of TCM treatments into COVID-19 management protocols.

The present study aims to address this knowledge gap by conducting a retrospective cohort study to assess the comparative efficacy of Lianhua Qingwen capsules combined with standard care versus standard care alone in patients with mild to moderate COVID-19. The primary objectives of this study are to evaluate the effects of Lianhua Qingwen on time to symptom improvement, time to viral clearance, 14-day clinical recovery rate, improvement in chest CT findings**,** and quality of life scores. Secondary objectives include assessing the impact of Lianhua Qingwen on inflammatory markers, immune function parameters**,** and the incidence of adverse events.

Methodology

Study population

This study was designed as a retrospective cohort study. Medical records from a hospital in China were reviewed for the period from 1 March 2023 to 31 December 2023. The study protocol received approval from the ethics committee of each participating institution, with a waiver of informed consent due to the retrospective nature of the study.

Inclusion and Exclusion criteria

Electronic medical records were screened to identify eligible and ineligible patients.

The inclusion criteria were as follows: aged 18–75 years; confirmed diagnosis of COVID-19 by a reverse transcription–polymerase chain reaction (RT-PCR) test; presenting with mild to moderate symptoms according to the World Health Organization (WHO) COVID-19 disease severity classification; time from symptom onset to enrolment ≤ 7 days; and willingness to participate and provide informed consent (where applicable). For this retrospective study, the requirement for individual informed consent was waived by the ethics committee due to the nature of the study. However, all patient data were anonymised and handled in strict compliance with ethical standards to protect patient privacy. The WHO classification defines mild cases as those with symptoms but without evidence of viral pneumonia or hypoxia**,** and moderate cases as those with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including $SpO_2 \geq 90\%$ on room air.

The exclusion criteria were as follows: patients with severe or critical COVID-19 requiring intensive care or mechanical ventilation; pregnant or breastfeeding women; patients with a known allergy to any component of Lianhua Qingwen capsules; patients with severe liver dysfunction (defined as alanine transaminase or aspartate transaminase > 5 times the upper limit of normal); patients with severe renal dysfunction (defined as estimated glomerular filtration rate < 30 mL/min/1.73 m²); patients who had participated in other clinical trials within 30 days before enrolment or had any condition that, in the opinion of the investigators, would compromise the safety of the patient or the quality of the study data.

Intervention

Treatment group protocol

Patients in the treatment group received Lianhua Qingwen capsules – four capsules, three times daily, orally, for 14 days. They also received standard care (as described below).

Control group protocol

Patients in the control group received standard care alone (as described below).

Standard care components

All patients in both groups received standard care according to the latest national and international guidelines for the management of mild to moderate COVID-19, which included the following:

a) Symptomatic treatment, comprising (i) antipyretics (e.g., acetaminophen) for fever > 38.5°C, (ii) antitussives for severe cough, and (iii) oral hydration and nutritional support.

b) Close monitoring of vital signs, oxygen saturation, and symptoms.

c) Oxygen therapy if $SpO_2 < 94\%$ on room air.

d) Prone positioning when appropriate.

e) Anticoagulation prophylaxis with low molecular weight heparin in patients with high D-dimer levels or other risk factors for thrombosis.

f) Treatment of comorbidities as per standard protocols

g) Psychological support

The use of other experimental treatments for COVID-19 was not allowed during the study period. Any additional medications or interventions were recorded in detail.

Outcome measures

Primary outcomes

a) Time to symptom improvement – defined as the time from randomisation to the 1st day of sustained improvement in major symptoms (fever, cough, and fatigue) for ≥ 72 hours. Symptom severity was assessed daily using a 4-point scale (0 = absent, 1 = mild, 2 = moderate, 3 = severe). Symptom improvement was scored by two independent clinical doctors who were trained to use the same scoring criteria. If there was a discrepancy between the two scorers, a third senior clinical doctor was consulted to make the final decision.

b) Time to viral clearance – defined as the time from randomisation to the first of two consecutive negative RT-PCR tests for SARS-CoV-2, with tests performed every other day.

c) Fourteen-day clinical recovery rate – defined as the proportion of patients achieving clinical recovery within 14 days of randomisation. Clinical recovery was defined as normal body temperature for ≥ 72 hours, resolution of respiratory symptoms, and two consecutive negative RT-PCR tests for SARS-CoV-2.

d) Improvement in chest CT findings – assessed by comparing baseline CT scans with follow-up scans on day 14. Improvement was defined as a reduction in the extent of lung involvement by at least two levels on a 5-point scale (0 = no involvement, 1 ≤ 25%, 2 = 25%–50%, 3 = 50%–75%, 4 ≥ 75% involvement). The CT scans were scored independently by two experienced radiologists who were blinded to the treatment allocation. In case of disagreement, a third radiologist was consulted for a final decision.

e) Quality of life scores – measured using the 36-Item Short Form Survey (SF-36) questionnaire at baseline and day 14. The SF-36 assesses eight domains of health-related quality of life, with higher scores indicating better quality of life.

Secondary outcomes

a) Changes in inflammatory markers:

Indicators – C-reactive protein (CRP), procalcitonin (PCT), and white blood cell (WBC) count.

Assessment method: blood samples were collected at baseline and on day 14 for analysis. All samples were tested in a standardised clinical laboratory using automated immunoassay and haematology analysers to ensure accuracy and reproducibility.

Data analysis: mixed-effects models were used to analyse the changes in inflammatory markers before and after treatment.

b) Immune function improvement:

Indicators – CD4+ T cell count, CD8+ T cell count, and natural killer (NK) cell activity.

Assessment method – blood samples were collected at baseline and on day 14. Flow cytometry was used to measure CD4+ and CD8+ T cell counts, and cytotoxicity assays were conducted to assess NK cell activity.

Data analysis – mixed-effects models were used to analyse the changes in immune function parameters before and after treatment.

c) Adverse event rate:

Indicators – incidence and severity of adverse events.

Assessment method – all adverse events occurring during the study period were recorded in detail. The severity of adverse events was assessed using the Common Terminology Criteria for Adverse Events v5.0.

Data analysis

Fisher's exact test was used to compare the incidence of adverse events between the two groups, and descriptive statistics were applied to analyse the types and severity of adverse events.

Statistical methods

All analyses were performed on the propensity-matched cohorts. Missing data were handled using multiple imputation when appropriate. Sensitivity analyses were performed to assess the robustness of the results to unmeasured confounding.

Continuous variables were summarised as means and standard deviations or medians and interquartile ranges (IQRs), depending on their distribution. Categorical variables were presented as frequencies and percentages. Baseline characteristics were compared between groups using Student's *t*-test or the Mann-Whitney U test for continuous variables and the chi-squared test or Fisher's exact test for categorical variables.

Time-to-event outcomes (time to symptom improvement and time to viral clearance) were analysed using Cox proportional hazards models, adjusted for stratification factors and relevant baseline characteristics. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated.

The 14-day clinical recovery rate and improvement in chest CT findings were compared between groups using chi-squared tests. Risk ratios and 95% CIs were calculated. Logistic regression models were used to adjust for potential confounders.

Changes in scores, inflammatory markers, and immune function parameters were analysed using

Table 1. Baseline Demographic and Clinical Characteristics.

Characteristic	Lianhua Qingwen (n = 142)	Placebo (n = 142)	*p*
Age, years (mean ± SD)	45.7 ± 13.2	46.3 ± 12.8	0.702
Gender, male (%)	77 (54.2%)	75 (52.8%)	0.811
BMI, kg/m² (mean ± SD)	24.8 ± 3.5	25.1 ± 3.7	0.476
Disease severity, n (%)			0.892
Mild	86 (60.6%)	88 (62.0%)	
Moderate	56 (39.4%)	54 (38.0%)	
Days from symptom onset (mean ± SD)	4.2 ± 1.8	4.3 ± 1.7	0.636
Comorbidities, n (%)			
Hypertension	31 (21.8%)	29 (20.4%)	0.767
Diabetes	18 (12.7%)	21 (14.8%)	0.604
Cardiovascular disease	12 (8.5%)	10 (7.0%)	0.658
Chronic lung disease	8 (5.6%)	9 (6.3%)	0.803
Symptoms at baseline, n (%)			
Fever	118 (83.1%)	121 (85.2%)	0.625
Cough	126 (88.7%)	124 (87.3%)	0.715
Fatigue	98 (69.0%)	101 (71.1%)	0.694
Dyspnea	45 (31.7%)	42 (29.6%)	0.695
Loss of taste or smell	67 (47.2%)	71 (50.0%)	0.631

Table 2. Cox Proportional Hazards Model Results for Primary Outcomes.

Outcome	Median Time (days)		Adjusted HR (95% CI)	*p*
	Lianhua Qingwen	Placebo		
Time to symptom improvement	5.7 (IQR: 4.2-7.3)	7.3 (IQR: 5.8-9.1)	1.43 (1.21-1.69)	< 0.001
Time to viral clearance	7.2 (IQR: 5.9-8.8)	9.8 (IQR: 7.6-11.5)	1.52 (1.28-1.80)	< 0.001

HR: Hazard Ratio; CI: Confidence Interval; IQR: Interquartile Range.

mixed-effects models to account for repeated measurements, with treatment group, time, and their interaction as fixed effects and patient as a random effect.

Adverse event rates were compared between groups using Fisher's exact test.

All statistical tests were two-sided, with a significance level of 0.05. Multiple comparisons for secondary outcomes were adjusted using the Benjamini–Hochberg method to control the false discovery rate. Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

Results

Baseline characteristics

After propensity score matching, 284 patients with mild to moderate COVID-19 were included (142 in the Lianhua Qingwen group, 142 in the control group). Baseline demographics, disease severity, comorbidities**,** and symptoms were well-balanced between groups (all $p > 0.05$, Table 1).

Primary outcome measures

Symptom improvement time

As shown in Table 2, the median time to symptom improvement was 5.7 days (IQR: 4.2–7.3) in the treatment group and 7.3 days (IQR: 5.8–9.1) in the control group. After adjustment using the Cox proportional hazards model, the HR for symptom improvement in the treatment group was 1.43 (95% CI: 1.21–1.69), $p < 0.001$. This indicates that the rate of symptom improvement was 43% faster in the treatment group than in the control group.

Time to viral clearance

As shown in Table 2, the median time to viral clearance was 7.2 days (IQR: 5.9–8.8) in the treatment group and 9.8 days (IQR: 7.6–11.5) in the control group. After adjustment using the Cox proportional hazards model, the HR for viral clearance in the treatment group was 1.52 (95% CI: 1.28–1.80), $p < 0.001$. This indicates that the rate of viral clearance was 52% faster in the treatment group than in the control group.

Fourteen-day clinical recovery rate

As shown in Table 3, the clinical recovery rate at 14 days was 91.5% ($n = 130$) in the treatment group and 82.4% ($n = 117$) in the control group. The risk ratio (RR) was 1.11 (95% CI: 1.01–1.22), $p = 0.024$. This indicates that the 14-day clinical recovery rate was significantly higher in the treatment group than in the control group.

Improvement in chest computed tomography findings

As shown in Table 3, the rate of improvement in chest CT findings was 78.9% ($n = 112$) in the treatment group and 64.8% ($n = 92$) in the control group. The RR was 1.22 (95% CI: 1.05–1.41), $p = 0.009$. This indicates that the improvement in chest CT findings was significantly better in the treatment group than in the control group.

Quality of life scores

Quality of life was assessed using the SF-36 questionnaire, with significant improvements observed in both the physical component summary (PCS) and the mental component summary (MCS) in the treatment group compared with the control group.

Table 3. Clinical Recovery Rate and CT Improvement.

Outcome	Lianhua Qingwen (n = 142)	Placebo (n = 142)	Risk Ratio (95% CI)	*p*
14-day clinical recovery	130 (91.5%)	117 (82.4%)	1.11 (1.01-1.22)	0.024
CT improvement at day 14	112 (78.9%)	92 (64.8%)	1.22 (1.05-1.41)	0.009

CI: Confidence Interval.

Table 4. Changes in SF-36 Scores from Baseline to Day 14.

SF-36 Component	Lianhua Qingwen (n = 142)	Placebo (n = 142)	Mean Difference (95% CI)	*p*
PCS change	10.2 ± 4.5	7.8 ± 4.2	2.4 (1.4-3.4)	< 0.001
MCS change	8.7 ± 3.9	6.5 ± 3.7	2.2 (1.3-3.1)	< 0.001

PCS: Physical Component Summary; MCS: Mental Component Summary; CI: Confidence Interval.

Table 5. Changes in Inflammatory Markers from Baseline to Day 7 and Immune Function Parameters from Baseline to Day 14.

Marker	Lianhua Qingwen (n = 142)	Placebo (n = 142)	Mean Difference (95% CI)	*p*
CRP (mg/L)	-18.5 ± 7.2	-14.1 ± 6.9	-4.4 (-6.1 to -2.7)	< 0.001
PCT (ng/mL)	-0.12 ± 0.06	-0.07 ± 0.05	-0.05 (-0.06 to -0.04)	< 0.001
WBC (× 10^9/L)	-2.1 ± 1.4	-0.8 ± 1.2	-1.3 (-1.6 to -1.0)	< 0.001
Parameter				
CD4 + T cells (/μL)	184 ± 62	123 ± 54	61 (47-75)	< 0.001
CD8 + T cells (/μL)	112 ± 41	67 ± 38	45 (35-55)	< 0.001
NK cell activity (%)	14.6 ± 5.2	9.1 ± 4.8	5.5 (4.3-6.7)	< 0.001

CRP: C-reactive protein; PCT: Procalcitonin; WBC: White blood cell count; CI: Confidence Interval; NK: Natural killer; CI: Confidence Interval.

PCS changes: the treatment group had a mean improvement of 10.2 points (± 4.5), whereas the control group had a mean improvement of 7.8 points (± 4.2). The mean difference was 2.4 points (95% CI: 1.4–3.4), $p < 0.001$ (Table 4).

MCS changes: the treatment group had a mean improvement of 8.7 points (± 3.9), whereas the control group had a mean improvement of 6.5 points (± 3.7). The mean difference was 2.2 points (95% CI: 1.3–3.1), $p < 0.001$ (Table 4).

Secondary outcomes

Changes in inflammatory markers:

CRP levels: the treatment group had a mean decrease of 18.5 mg/L (± 7.2) from baseline, whereas the control group had a mean decrease of 14.1 mg/L (± 6.9). The mean difference was −4.4 mg/L (95% CI: −6.1–−2.7), $p < 0.001$ (Table 5).

PCT levels: the treatment group had a mean decrease of 0.12 ng/mL (± 0.06) from baseline, whereas the control group had a mean decrease of 0.07 ng/mL (± 0.05). The mean difference was −0.05 ng/mL (95% CI: −0.06–−0.04), $p < 0.001$ (Table 5).

WBC count: the treatment group had a mean decrease of 2.1 × 10^9/L (± 1.4) from baseline, whereas the control group had a mean decrease of 0.8 × 10^9/L (± 1.2). The mean difference was −1.3 × 10^9/L (95% CI: −1.6–−1.0), $p < 0.001$ (Table 5).

Immune function improvement:

CD4+ T cell count: the treatment group had a mean increase of 184 cells/μL (± 62) from baseline, whereas the control group had a mean increase of 123 cells/μL (± 54). The mean difference was 61 cells/μL (95% CI: 47–75), $p < 0.001$ (Table 5).

CD8+ T cell count: the treatment group had a mean increase of 112 cells/μL (± 41) from baseline, whereas the control group had a mean increase of 67 cells/μL (± 38). The mean difference was 45 cells/μL (95% CI: 35–55), $p < 0.001$ (Table 5).

NK cell Activity: T

The treatment group had a mean increase of 14.6% (± 5.2) from baseline, whereas the control group had a mean increase of 9.1% (± 4.8). The mean difference was 5.5% (95% CI: 4.3–6.7), $p < 0.001$ (Table 5).

Adverse event rate

The incidence of adverse events was 12.7% ($n = 18$) in the treatment group and 13.4% ($n = 19$) in the control group, with no significant difference between the two groups ($p = 0.856$). Specific adverse events included nausea, diarrhoea, headache, dizziness, and rash, with no significant differences in the incidence of these adverse events between the two groups ($p > 0.05$) (Table 6).

Discussion

This study provides compelling evidence for the efficacy and safety of Lianhua Qingwen capsules as an adjunctive treatment for mild to moderate COVID-19 [16,19]. The results demonstrate significant improvements across multiple clinically relevant outcomes, including symptom resolution, viral clearance, radiological improvement**,** and quality of life measures. These results are comparable and consistent with previous research findings, and they have significant implications for the management of COVID-19 as well as the potential role of TCM in addressing global health challenges [9,20].

Symptom improvement and viral clearance

One of the most striking findings of this study is the significant reduction in time to symptom improvement

Table 6. Adverse Events.

Adverse Event	Lianhua Qingwen (n = 142)	Placebo (n = 142)	*p*
Any adverse event	18 (12.7%)	19 (13.4%)	0.856
Nausea	7 (4.9%)	8 (5.6%)	0.788
Diarrhea	5 (3.5%)	6 (4.2%)	0.758
Headache	4 (2.8%)	3 (2.1%)	0.702
Dizziness	2 (1.4%)	1 (0.7%)	0.562
Skin rash	1 (0.7%)	2 (1.4%)	0.562

and viral clearance in the Lianhua Qingwen group compared with the placebo group. The HRs of 1.43 for symptom improvement and 1.52 for viral clearance indicate that patients treated with Lianhua Qingwen had a 43% higher probability of symptom improvement and a 52% higher probability of viral clearance at any given time point. These results are clinically meaningful, as faster symptom resolution and viral clearance can lead to reduced transmission risk, shorter isolation periods, and improved patient well-being [3,17]. Compared with the efficacy of antiviral drugs (such as remdesivir), Lianhua Qingwen capsules have shown comparable or even better effects in symptom relief and virus clearance. Beigel *et al.* [1] demonstrated that remdesivir can shorten the recovery time of hospitalised patients; however, its efficacy is limited in patients with mild to moderate disease. In contrast, Lianhua Qingwen capsules have shown good efficacy in outpatient treatment, with no serious adverse reactions observed.

The mechanisms underlying these effects may be multifaceted. Previous studies have shown that Lianhua Qingwen possesses broad-spectrum antiviral properties, including direct inhibition of viral replication and modulation of host immune responses [10,21]. The combination of multiple herbs in Lianhua Qingwen may provide a synergistic effect, targeting various aspects of viral pathogenesis and host defence mechanisms simultaneously [15,22].

Clinical recovery and radiological improvement

The higher 14-day clinical recovery rate observed in the Lianhua Qingwen group (91.5% vs 82.4%) suggests that the treatment accelerates the overall recovery process. This finding is particularly important in the context of healthcare system capacity, as faster recovery can lead to reduced hospitalisation duration and improved resource utilisation [17,23].

The more pronounced improvement in chest CT findings in the Lianhua Qingwen group (78.9% vs 64.8%) is also noteworthy. This is similar to the findings of Ding *et al.* [9], who discovered that Lianhua Qingwen capsules can significantly increase the clinical cure rate and radiological improvement rate of patients.

Compared with other international COVID-19 treatment regimens, the efficacy of Lianhua Qingwen capsules in patients with mild to moderate disease is particularly remarkable. For example, some antiviral drugs (such as hydroxychloroquine) commonly used in Western countries have failed to show significant clinical benefits in multiple studies [24], whereas Lianhua Qingwen capsules have demonstrated clear efficacy in this study. Radiological improvement is a crucial indicator of disease resolution in COVID-19, reflecting the attenuation of lung inflammation and tissue repair. The superior performance of Lianhua Qingwen in this aspect suggests that it may have specific anti-inflammatory effects in the respiratory system, consistent with its traditional use in treating respiratory infections [15,25].

Quality of life and patient-reported outcomes

The significant improvements in SF-36 scores, in both the physical and mental components, highlight the positive impact of Lianhua Qingwen on patients' overall well-being. This holistic improvement aligns with the TCM philosophy of treating the whole person rather than just the disease. The enhanced quality of life reported by patients in the Lianhua Qingwen group may be attributed to faster symptom resolution, reduced anxiety due to quicker recovery, and potential mood-enhancing effects of some herbal components [19,26].

Inflammatory markers and immune function

The more rapid decrease in inflammatory markers (CRP, PCT, WBC) and the enhanced immune function parameters (CD4+ T cells, CD8+ T cells, NK cell activity) in the Lianhua Qingwen group provide insights into the potential mechanisms of action of this herbal formula. These findings suggest that Lianhua Qingwen may exert its therapeutic effects through immunomodulation and anti-inflammatory actions [16,27]. This is consistent with the findings of Lee *et al.* [15], who pointed out that Lianhua Qingwen capsules exert antiviral and anti-inflammatory effects by modulating immune responses and inhibiting cytokine storms.

The ability to balance the immune response is particularly crucial in COVID-19, where both insufficient and excessive immune activation can lead to poor outcomes [28]. The observed improvements in T cell counts and NK cell activity indicate that Lianhua Qingwen may help restore immune homeostasis, potentially contributing to more effective viral clearance and tissue repair [10].

Safety profile

The comparable safety profile between the Lianhua Qingwen and placebo groups is reassuring and consistent with previous studies on the long-term use of this herbal formula for respiratory infections [23,29]. The absence of serious adverse events and the similar incidence of mild side effects suggest that Lianhua Qingwen can be safely administered as an adjunct to standard care in patients with COVID-19 [17,26].

Strengths and limitations

This study has several strengths, including its multicentre nature, careful propensity score matching to minimise selection bias, and comprehensive assessment of outcomes. However, some limitations should be acknowledged. First, as a retrospective study, the findings may be subject to residual confounding despite careful matching. Second, although the 14-day follow-up period was sufficient to assess short-term outcomes, longer-term effects and potential late complications were not evaluated. Future studies with extended follow-up periods would be valuable in this regard.

Third, the study focused on mild to moderate COVID-19 cases, and the efficacy of Lianhua Qingwen in severe or critical cases remains to be determined. Finally, although our results suggest potential mechanisms of action, more detailed pharmacological studies are needed to fully elucidate how Lianhua Qingwen exerts its therapeutic effects.

Implications for clinical practice and future research

The findings of this study have several important implications for clinical practice and research. First, the positive results support the potential integration of evidence-based TCM treatments, such as Lianhua Qingwen, into mainstream COVID-19 management protocols, particularly for mild to moderate cases. This integration aligns with the concept of personalised medicine, as the multi-component nature of Lianhua Qingwen addresses multiple aspects of the disease simultaneously, suggesting that future research could explore whether certain subgroups of patients benefit more from this treatment approach. Moreover, the efficacy of Lianhua Qingwen highlights the potential of multi-target herbal formulations in treating complex diseases, such as COVID-19, which may inspire new approaches in drug discovery and development. Last, the successful application of a TCM formula in treating a global pandemic underscores the importance of cross-cultural medical exchanges and the potential benefits of integrating diverse healing traditions into global health strategies.

Future research directions stemming from this study are multifaceted and promising. Mechanistic studies to identify the active compounds in Lianhua Qingwen and their specific molecular targets would provide valuable insights into its mode of action. Additionally, trials assessing the efficacy of Lianhua Qingwen in preventing progression to severe COVID-19 in high-risk populations could expand its potential applications. Combination studies evaluating Lianhua Qingwen with other promising COVID-19 treatments, such as antivirals or immunomodulators, may lead to more effective therapeutic strategies. Finally, investigating Lianhua Qingwen's potential role in addressing long COVID or post-acute sequelae of SARS-CoV-2 infection could open new avenues for managing the long-term health consequences of COVID-19. These research directions collectively aim to further elucidate the full potential of Lianhua Qingwen in the comprehensive management of COVID-19 and its aftermath.

Conclusions

Lianhua Qingwen capsules represent a safe and effective adjunctive treatment for mild to moderate COVID-19, offering a valuable addition to the current therapeutic arsenal. As the global community continues to grapple with the challenges posed by the COVID-19 pandemic and its evolving variants, the integration of evidence-based traditional medicines, such as Lianhua Qingwen, may provide new avenues for enhancing patient care and public health outcomes.

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Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Changde Hospital, Xiangya School of Medicine, Central South University (The First People's Hospital of Changde City). With a waiver of informed consent due to the retrospective nature of the study.

Availability of data and materials

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Authors' contributions

Yang YM conceived of the study, and Yang YM and Zhou M participated in its design and data analysis, and statistics, and Yang YM and Zhou M helped to draft the manuscript. All authors read and approved the final manuscript.

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Conflict of interest

No conflict of interest is declared.

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