Systematic Review and Meta-Analysis

Medicine®

OPEN

Efficacy and safety of Lianhuaqingwen for mild or moderate coronavirus disease 2019

A meta-analysis of randomized controlled trials

Zheng Fan, MM[a], Guiming Guo, MM[a], Xiaoping Che, MM[a], Ying Yang, MD[a], Yang Liu, MM[a], Luyang Li, MM[a], Xinyu Chang, MD[a], Lijuan Han, MM[a], Xiaorong Cai, MM[a], Huilin Tang, MS[b,*]

Abstract

Background : Coronavirus disease 2019 (COVID-19) is an emerging and rapidly evolving disease, with no recommended effective anti-coronavirus treatments. Traditional Chinese Medicine (TCM) has been widely used to treat COVID-19 in China, and the most used one is Lianhuaqingwen (LH). This study aimed to assess the efficacy and safety of LH combined with usual treatment vs usual treatment alone in treating mild or moderate COVID-19 by a meta-analysis of randomized controlled trials (RCTs).

Methods and analysis : We systematically searched the Medline (OVID), Embase, the Cochrane Library, and 4 Chinese databases from inception to July 2020 to include the RCTs that evaluated the efficacy and safety of LH in combination with usual treatment vs usual treatment for mild or moderate COVID-19. A meta-analysis was performed to calculate the risk ratio (RR) and 95% confidence interval (CI) for binary outcomes and mean difference (MD) for continuous outcomes.

Results : A total of 5 RCTs with 824 individuals with mild or moderate COVID 19 were included. Compared with the usual treatment alone, LH in combination with usual treatment significantly improved the overall clinical efficacy (RR = 2.39, 95% CI 1.61–3.55), increased the rate of recovery of chest computed tomographic manifestations (RR = 1.80, 95% CI 1.08–3.01), reduced the rate of conversion to severe cases (RR = 0.47, 95% CI 0.29–0.74), shorten the duration of fever (MD = −1.00, 95% CI −1.17 to −0.84). Moreover, LH in combination with usual treatment did not increase the occurrence of the adverse event compared to usual treatment alone.

Conclusion : Our meta-analysis of RCTs indicated that LH in combination with usual treatment may improve the clinical efficacy in patients with mild or moderate COVID-19 without increasing adverse events. However, given the limitations and poor quality of included trials in this study, further large-sample RCTs or high-quality real-world studies are needed to confirm our conclusions.

Abbreviations: CI = confidence interval, COVID-19 = coronavirus disease 2019, FEM = fixed-effects model, LH = Lianhuaqingwen, MD = mean difference, RCT = randomized controlled trial, REM = random-effects model, RR = risk ratio, TCM = Traditional Chinese Medicine.

Keywords: coronavirus disease 2019, efficacy outcomes, Lianhuaqingwen, meta-analysis, randomized controlled trials, safety outcomes

1. Introduction

As of July.1, 2020, coronavirus disease 2019 (COVID-19)[1] has resulted in more than 10 million cases and more than 500 000 deaths worldwide.[2] The worldwide spread of COVID-19 represents a profound threat to human health. However, currently, no specific anti-coronaviral drugs have been approved for the treatment of COVID-19, and no vaccine is available for preventing COVID-19. As of May 27, 2020, the interim guideline of World Health Organization recommend that chloroquine and hydroxychloroquine (+/- azithromycin), lopinavir/ritonavir, remdesivir, tocilizumab, interferon-β-1a, not be administered as treatment or prophylaxis for COVID-19, and safe supportive therapies were the cornerstone of therapy for patients.[3]

In China, Traditional Chinese Medicine (TCM) has a long history and has played an important role in the prevention and treatment of serious epidemic diseases.[4–6] According to the *Diagnosis and Treatment Protocol for Coronavirus Pneumonia (Trial version 7)*, Lianhuaqingwen (LH), a Traditional Chinese Patent Medicine formula including 13 herbs (Table 1), has been recommended by the National Health Commission for the treatment of COVID-19.[7] One prospective multicenter, ran-

Editor: Jorddy Neves Cruz.

The authors have no funding and conflicts of interests to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

[a] Department of Clinical Pharmacy, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, [b] Institute for Drug Evaluation, Peking University Health Science Center, Beijing, PR China.

[*] Correspondence: Huilin Tang, Institute for Drug Evaluation, Peking University Health Science Center, No 49 North Garden Road, Haidian District, Beijing 100191, PR China (e-mail: huiltang85@gmail.com).

How to cite this article: Fan Z, Guo G, Che X, Yang Y, Liu Y, Li L, Chang X, Han L, Cai X, Tang H. Efficacy and safety of Lianhuaqingwen for mild or moderate coronavirus disease 2019: a meta-analysis of randomized controlled trials. Medicine 2021;100:21(e26059).

Received: 1 August 2020 / Received in final form: 1 March 2021 / Accepted: 29 April 2021

http://dx.doi.org/10.1097/MD.0000000000026059

Table 1

The formulation of LH.

Local Name	Herb	Medicinal parts	Notes
Ma Huang	Ephedra sinica Stapf.	Herbaceous stem	
Ku Xing Ren	Prunus armeniaca L.	Seed	1. The China State Food and Drug Administration approved LH in 2004.
Lian Qiao	Forsythia suspensa (Thunb.)Vahl.	Fruit	
Bo He	Mentha haplocalyx Briq.	Herba	
Ban Lan Gen	Isatis indigotica Fort.	Roots	
Yu Xing Cao	Houttuynia cordata Thunb.	Herba	
Guan Zhong	Dryopteris crassirhizoma Nakai.	Rhizome	2.LH were manufactured Shijiazhuang Yiling Pharmaceutical Co. Ltd.
Jin Yin Hua	Lonicera japonica Thunb.	Flower	
Shi Gao	Gypsum fibrosum	Mineral substance	
Da Huang	Rheum palmatum L.	Roots and rhizomes	3.LH have two formulations: capsule and granule
Guang Huo Xiang	Pogostemon cablin (Blanco)) Benth.	Herba	
Hong Jing Tian	Rhodiola crenulata (Hook.f.et Thoms.) H.Ohba.	Roots and rhizomes	
Gan Cao	Glycyrrhiza uralensis Fisch.	Roots and rhizomes	

domized controlled trial (RCT) involving 284 patients with COVID-19 had shown that LH plus usual treatment could significantly improve the recovery rate (91.5% vs 82.4%) and short the time to symptom recovery (median: 7 days vs 10 days) as compared to usual treatment only.[8] However, an individual trial was limited by the small number of patients included. Therefore, we performed this study to evaluate the efficacy and safety of LH in combination with usual treatment vs usual treatment alone in treating COVID-19 by a meta-analysis of available evidence from randomized trials.

2. Methods

This meta-analysis was performed and reported according to Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA). Patient consent and ethical approval were not required for this study because it was a meta-analysis of published studies.[9]

2.1. Search strategy

We systematically searched Medline (OVID), Embase, the Cochrane Library, and 4 Chinese databases (including China National Knowledge Infrastructure (CNKI) database, Wanfang Data Knowledge Service Platform, Chinese Biomedicine Literature Database, and Chinese Sci-tech Journals Database) from inception to July 2020 using relevant search terms. The search strategy of PubMed was presented in Table 2. We limited the language of articles to English and Chinese only. We also manually searched the reference list of the included studies and ClinicalTrials.gov as a supplementary source for the literature search.

2.2. Study selection and outcome measures

Three investigators (ZF, YY, and YL) independently selected eligible studies according to the predefined inclusion criteria and exclusion criteria. Included trials must meet the following criteria:

1. RCTs or randomized crossover trials (RTs);
2. Laboratory-confirmed and suspected cases with COVID-19;
3. Patients aged 18 years or greater;
4. The interventional group was LH in combination with usual treatment, and the control group was usual treatment alone.

The trials would be excluded if:

1. duplicates;
2. reviews and conference abstracts;
3. severe COVID-19 patients;
4. severe systemic diseases (i.e., malignancy, autoimmune diseases, liver or renal diseases);
5. asthma or other chronic airway diseases needing maintenance therapy, acute respiratory tract bacterial infection (i.e., bronchiectasis, tonsillitis, bronchitis, rhinosinusitis, otitis media), severe pulmonary interstitial diseases;
6. women during pregnancy or lactation.

Table 2

Example of PubMed search strategy.

Number	Search Terms
1	Mesh descriptor: (Lianhuaqingwen) explode all trees
2	((((((Lian-Hua Qing-Wen [Title/Abstract]) OR Lianhuaqingwen Capsule [Title/Abstract]) OR LianHua QingWen [Title/Abstract]) OR Lianhua Qingwen [Title/Abstract]) OR Lianhuaqingwen granule [Title/Abstract])
3	Or 1–2
4	Mesh descriptor: (COVID-19) explode all trees
5	((((((2019 novel coronavirus infection[Title/Abstract] OR 2019-nCoV infection[Title/Abstract]) OR COVID-19 pandemic[Title/Abstract]) OR coronavirus disease-19[Title/Abstract]) OR 2019-nCoV disease[Title/Abstract]) OR COVID19[Title/Abstract]) OR 2019 novel coronavirus disease[Title/Abstract]) OR coronavirus disease 2019[Title/Abstract]
6	Or 4–5
7	3 and 6

We screened the titles and abstracts for potential studies in the first screening and then reviewed the full texts of these potential studies in the second screening. The primary outcomes included overall clinical efficacy and safety outcomes, and the secondary outcomes included the conversion to severe cases, the duration of fever, and improvement in chest computed tomographic manifestations. The overall clinical efficacy was defined as the complete resolution of fever, fatigue, and coughing.[8] Any disagreements were resolved through discussion, and if necessary, a third investigator (HT) was consulted.

2.3. Data extraction and quality assessment

Three reviewers (ZF, YY, and YL) extracted the data according to a predesigned data-collection form. We included the following data: authors, publication year, participant characteristic (participation eligibility criteria, gender, and age), intervention information, and outcomes of interest. We assessed the risk of bias of included RCTs and RTs using the Cochrane risk of bias assessment tool.[10] In the case of missing data, we contacted the authors of eligible studies for clarifications. Any disagreements about data extraction and quality assessment were resolved through discussion among all authors.

2.4. Statistical analysis

We compared the treatment effect through meta-analysis in an intention to treat manner (following the allocation of participants in studies). We calculated the mean differences (MDs) and their 95% confidence intervals (CIs) for continuous outcomes and risk ratios (RRs) for binary outcomes. Statistical heterogeneity was assessed using the Chi-Squared test and I^2 test. We used a fixed-effects model (FEM) if $I^2 < 50\%$, otherwise, a random-effects model (REM) was used. A funnel plot was performed to assess the publication bias if more than 8 trials were included, accordingly no publication bias assessment was performed due to only 5 trials included in this study performed. The data analysis was performed using RevMan version 5.3 software and $P < .05$ was considered statistically significant.

3. Results

3.1. Search results

Fifty two relevant records were retrieved from the electronic databases and 27 records were left after removing duplicates. Of these, 20 were excluded after title/abstract screening and 7 reports were eligible for full-text review. After full-text review, we excluded 2 reports for the following reason: 2 studies did not compare LH in addition to usual treatment with usual treatment alone. Finally, we included 5 articles involving 824 patients.[8,11–14] The process of literature search and study selection was presented in Figure 1.

3.2. Study characteristics and quality assessment

The basic characteristics of the 5 trials were presented in Table 3. Of the 824 patients with mild or moderate COVID-19, 448 were

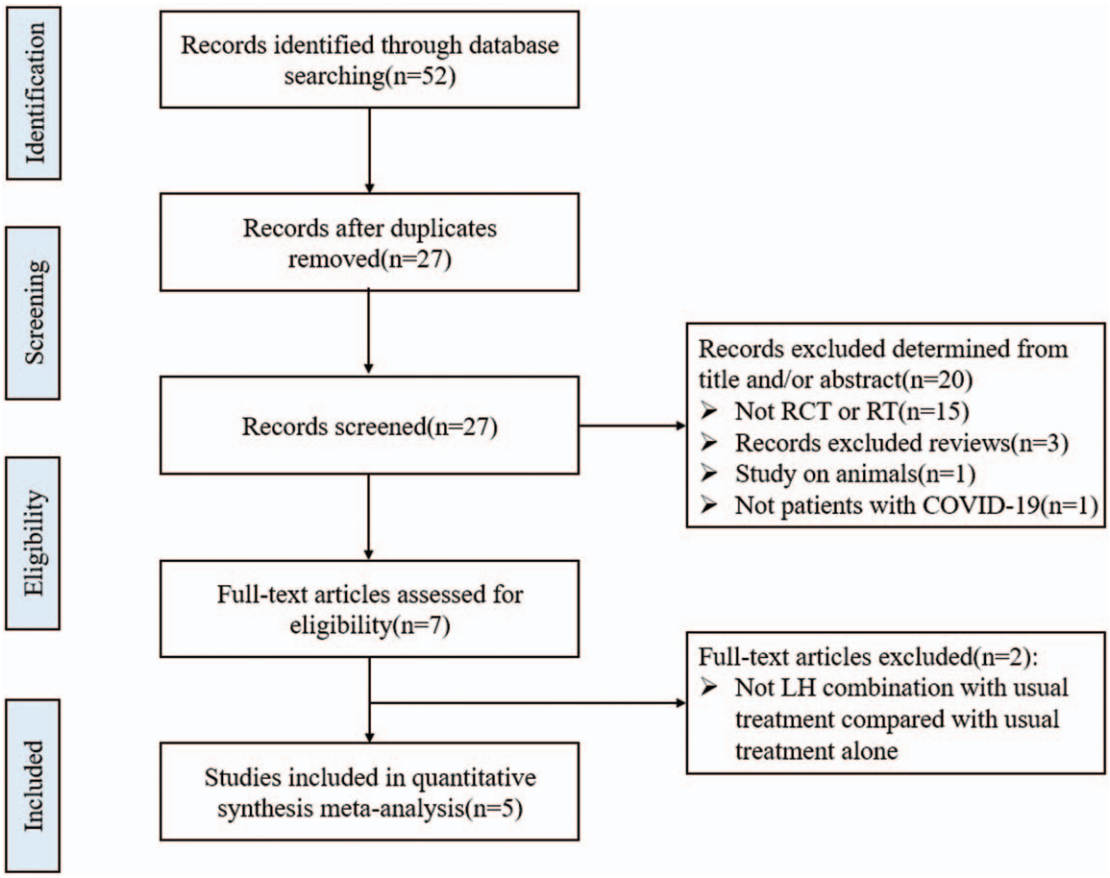

Figure 1. Flowchart of study selection.

Table 3

Characteristics of included studies.

	Patients				Intervention			
Studies	Disease	T/C	M/F	Age (years)	Treatment group	Control group	Duration (days)	Outcomes
Hu 2020	Confirmed	142/142	150/134	≥18	LH capsules (4 capsules thrice daily) in combination with usual treatment	usual treatment including oxygen therapy, antiviral medications, and symptomatic therapies	14	01,02,03,04,05,
Yu 2020	Confirmed	147/148	171/124	18-75	LH granules (1 packet thrice daily) in combination with usual treatment	usual treatment including abidol (0.2g, tid)+ moxifloxacin (0.4g,qd)+ ambroxol (30 mg,tid)	7	01, 02, 04,
Lv 2020	Suspected	63/38	46/55	≥18	LH granules (1 packet thrice daily) in combination with usual treatment	usual treatment including nutritional support, symptomatic treatment, antiviral and antibiotic drug treatment	10	02,05
Cheng 2020	Confirmed	51/51	53/49	18-70	LH granules (1 packet thrice daily) in combination with usual treatment	usual treatment including nutritional support, symptomatic treatment, antiviral and antibiotic drug treatment	7	01, 02,03,04,
Yao 2020	Confirmed	21/21	28/14	≥18	LH granules (1 packet thrice daily) in combination with usual treatment	usual treatment recommended in the Diagnosis and Treatment Protocol for Coronavirus Pneumonia (Trial version 4)	—	03

T = treatment group, C = control group, 01 = overall clinical efficacy, 02 = conversion to severe cases, 03 = the duration of fever, 04 = improvement in chest computed tomographic manifestations, 05 = safety, —, unclear.

males and 376 were females, with ages ranging from 18 to 75 years. All 5 trials were performed in China. Usual treatment generally involved supportive treatment such as oxygen therapy, antiviral medications, and symptomatic therapies. The dose of LH was 4 capsules thrice daily[8] or 1 packet thrice daily.[11–14] The duration of treatment were 7 days,[11,13] 10 days[12], and 14 days[8].

Of the 5 trials included, 4 trials[8,11,13,14] reported random sequence generation. Only one trial[8] reported allocation concealment and blinding (outcome assessor). No blinding (participants) was implemented in all trials. None of the included trials had selective reporting. All trials have a low risk of incomplete outcome data. And, the baseline data of all trials was comparative (Fig. 2).

3.3. Efficacy outcomes

3.3.1. Overall clinical efficacy. Of the 5 trials included, 3 trials[8,11,13] with 681 cases reported the overall clinical efficacy of LH combination with usual treatment. There was no statistical heterogeneity among the trials ($P = .92$, $I^2 = 0\%$). Therefore, the data were synthesized using FEM. Meta-analysis showed that LH in combination with usual treatment could significantly improve

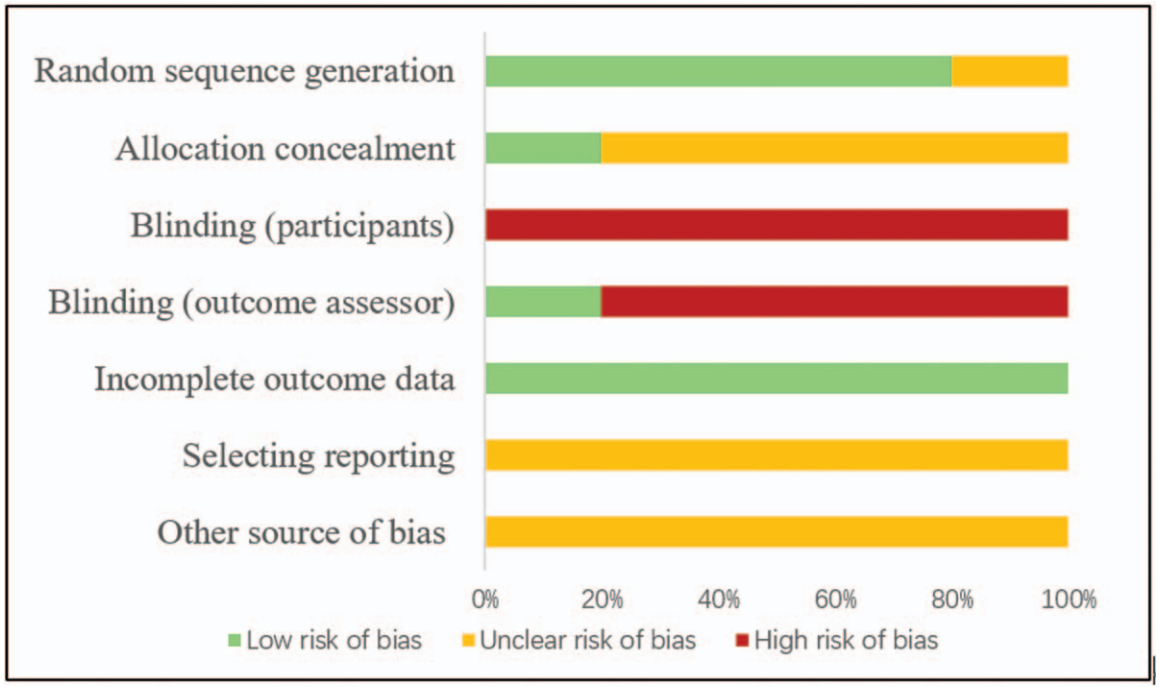

Figure 2. Summary of risk of bias assessment of each trial.

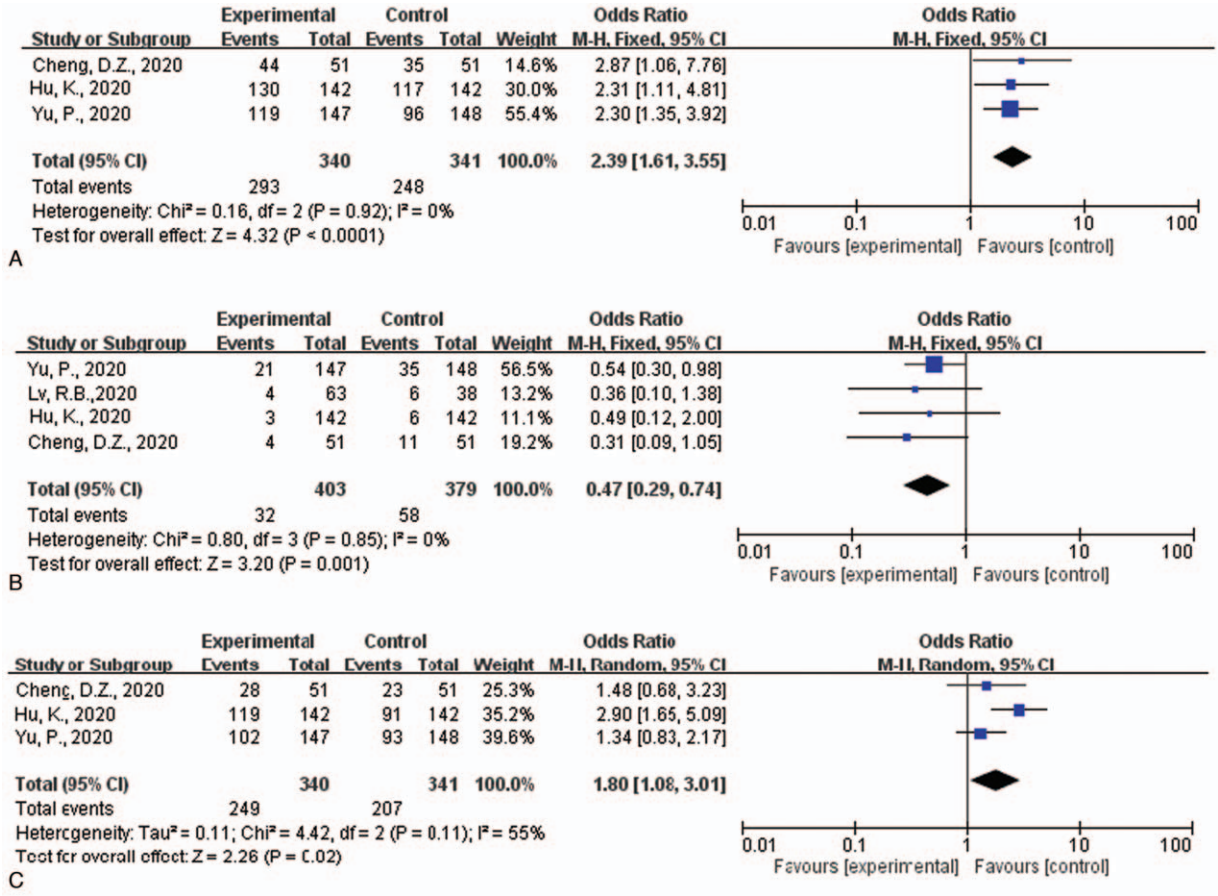

Figure 3. Effects of Lianhuaqingwen in combination with usual treatment on the following outcomes (A) overall clinical efficacy; (B) conversion to severe cases; (C) improvement in chest computed tomographic manifestations compared to usual treatment only in patients with mild or moderate COVID-19. COVID-19 = coronavirus Disease 2019.

the overall clinical efficacy as compared to usual treatment alone (RR = 2.39, 95% CI 1.61–3.55, $P < .0001$) (Fig. 3A).

3.3.2. The conversion to severe cases. Four trials[8,11,12,13] involving 782 cases reported the rate of the conversion to severe cases There was no statistical heterogeneity among the trials ($P = .85$, $I^2 = 0\%$). The meta-analysis using FEM showed that LH in combination with usual treatment was significantly associated with a lower rate of conversion to severe cases than usual treatment alone (RR = 0.47, 95% CI 0.29–0.74, $P = .001$) (Fig. 3B).

3.3.3. Improvement in chest computed tomographic manifestations. Three trials[8,11,13] with 456 cases reported the rate of improvement in chest computed tomographic manifestations. There was statistical heterogeneity among the trials ($P = .11$, $I^2 = 55\%$). Therefore, the data were synthesized using REM. Meta-analysis showed that LH in combination with usual treatment was significantly associated with a higher rate of improvement in chest computed tomographic manifestations as compared with usual treatment alone (RR = 1.80, 95% CI 1.08–3.01, $P < .05$) (Fig. 3C).

3.3.4. The duration of fever. Three trials[8,13,14] with 387 cases reported the duration of fever. There was no statistical heterogeneity among the trials ($P = .85$, $I^2 = 0\%$). Therefore, the data were synthesized using FEM. Meta-analysis showed that LH in combination with usual treatment could significantly shorten the duration of fever as compared to treatment alone [MD = −1.00, 95% CI −1.17, −0.84, Z = 11.77, $P < .0001$] (Fig. 4).

3.4. Safety outcomes

Two studies[8,12] reported adverse events during the follow-up periods. There was statistical heterogeneity among the trials ($P = .08$, $I^2 = 68\%$). Therefore, the data were synthesized using REM. Meta-analysis showed that there was no statistical significance between LH in combination with usual treatment and usual treatment alone (RR = 0.43, 95% CI 0.12–1.54, $P = .19$) (Fig. 5).

4. Discussion

To our knowledge, this is the first meta-analysis of randomized trials to evaluate the efficacy and safety of LH in combination with usual treatment for the treatment of COVID-19. Our results showed that LH in combination with usual treatment could significantly improve overall clinical efficacy, decrease the rate of

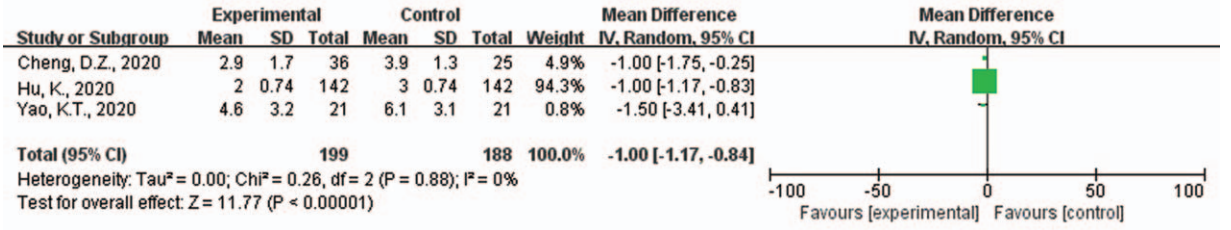

Figure 4. Effects of Lianhuaqingwen in combination with usual treatment on the duration of fever compared to usual treatment only in patients with mild or moderate COVID-19.

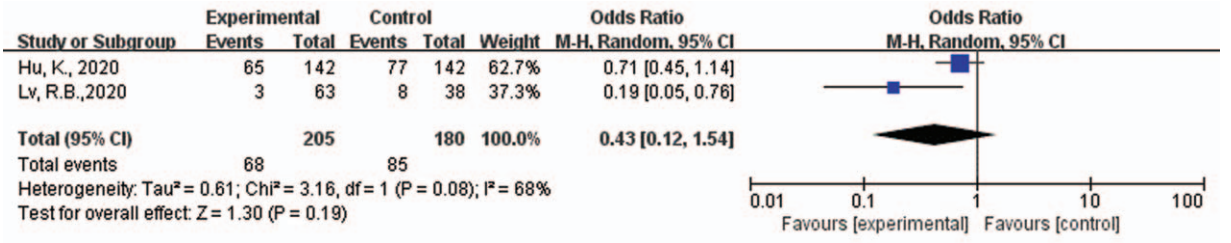

Figure 5. Effects of Lianhuaqingwen in combination with usual treatment on adverse events compared to usual treatment only in patients with mild or moderate COVID-19.

conversion to severe cases, shorten the duration of fever, and increase the rate of improvement in chest computed tomographic manifestations compared to usual treatment alone. Moreover, LH in combination with usual treatment did not increase the occurrence of adverse events as compared to usual treatment alone.

During the development of the COVID-19 epidemic in China, TCM was widely used in treating COVID-19,[15] and was included in the guidelines for the diagnosis and treatment of COVID-19.[7] A total of 60,107 confirmed cases (more than 85% of COVID-19 patients) used TCM to treat COVID-19.[16] Among the commonly used TCMs, the most used one is LH. LH, which is a patented product, has been marketed since the outbreak of SARS in 2003 in China. LH which could suppress the replication of SARS-CoV,[17] H3N2, H1N1, and H7N9 in vitro,[18–21] has been endorsed by the National Health Commission for the treatment of SARS, MERS, influenza, and human infection with H7N9 avian influenza.[22–25] Previous research has shown that LH conferred suppression of the cytopathic effect of SARS-CoV-2 in vitro and reduced the viral loads in the cytoplasm and cellular membrane,[26] and regulated immune response to viral infection,[19] anti-inflammation,[27] anti-acute lung injury.[28] A series of studies have also been carried out to explore the targets and signaling pathways of LH for treating COVID-19 and explore its underlying mechanism.[29,30] LH was shown to have an anti-virus (coronavirus) effect, antipyretic and analgesic effect, immune-regulation, anti-inflammation, and anti-acute lung injury.[31]

There were some limitations in this study. Firstly, we only searched Chinese and English databases; all included trials were carried out in China. Secondly, the risk of bias of included trials was high. Only one trial clearly described the allocation concealment. No blinding was implemented in all trials because of the urgency of the outbreak that entailed a timely treatment, and a placebo-controlled trial would be unethical considering the rapid outbreak of communicable diseases such as COVID-19. Thirdly, statistical heterogeneity across trials was observed in some meta-analyses, which might be caused by differences in the usual treatment used and dose and duration of LH. However, we cannot further explore the source of heterogeneity using meta-regression or subgroup analysis due to the limited number of included studies. Finally, due to only 5 trials included in this meta-analysis, we did not perform a publication bias assessment, thus we cannot exclude the potential publication bias in this study.

In summary, the available evidence from available randomized trials showed that in patients with mild or moderate COVID-19, LH in combination with usual treatment might improve the clinical efficacy, decrease the rate of conversion to severe cases, shorten the duration of fever, and increase the rate of improvement in chest computed tomographic manifestations compared to usual treatment alone. However, given the limitations and poor quality of included trials in this study, further large-sample RCTs or high-quality real-world studies are needed to confirm our conclusions.

Author contributions

Conceptualization: Guiming Guo, Xiaoping Che, Luyang Li, Huilin Tang.
Data curation: Ying Yang, Yang Liu.
Formal analysis: Lijuan Han, Xiaorong Cai.
Writing – original draft: Zheng Fan, Xinyu Chang.
Writing – review & editing: Huilin Tang.

References

[1] World Health Organization. Coronavirus disease 2019 (COVID-19) situation report – 22. World Health Organization, Geneva, 2020.

[2] World Health Organization. Coronavirus disease 2019 (COVID-19) situation report – 163. World Health Organization, Geneva, 2020.
[3] World Health Organization. Clinical management of COVID-19: Interim guidance. World Health Organization, Geneva, 2020.
[4] Lau JT, Leung PC, Wong EL, et al. The use of an herbal formula by hospital care workers during the severe acute respiratory syndrome epidemic in Hong Kong to prevent severe acute respiratory syndrome transmission, relieve influenza-related symptoms, and improve quality of life: a prospective cohort study. J Altern Complement Med 2005;11:49–55.
[5] Hsu CH, Hwang KC, Chao CL, et al. The lesson of supplementary treatment with Chinese medicine on severe laboratory-confirmed SARS patients. Am J Chin Med 2006;34:927–35.
[6] Wang C, Cao B, Liu QQ, et al. Oseltamivir compared with the Chinese traditional therapy maxingshigan-yinqiaosan in the treatment of H1N1 influenza: a randomized trial. Ann Intern Med 2011;155:217–25.
[7] National Health Commission of the People's Republic of China. Diagnosis and treatment protocol for coronavirus pneumonia (Trial version 7). National Health Commission of the People's Republic of China, Beijing, 2020.
[8] Hu K, Guan WJ, Bi Y, et al. Efficacy and safety of Lianhuaqingwen capsules, a repurposed Chinese herb, in patients with coronavirus disease 2019: A multicenter, prospective, randomized controlled trial. Phytomedicine, https://doi.org/10.1016/j.phymed.2020.153242.
[9] Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement– https://www.bmj.com/content/339/bmj.b2535.
[10] Higgins JP, Altman DG, Gotzsche PC. The Cochrane collaboration's tool for assessing risk of bias in randomized trials. BMJ 2011;343:d5928.
[11] Yu P, Li YZ, Wan SB, Wang Y. Observation on the Therapeutic effect of Lianhua Qingwen granule combined with Abidole in the treatment of mild COVID-19. Chinese Pharmaceutical Journal. http://kns.cnki.net/kcms/detail/11.2162.R.20200422.1429.002.html.
[12] Lv RB, Wang WJ, Li X. Clinical observation on s lianhua qingwen granules combined with western medicine conventional therapy in the treatment of 63 suspected cases of coronavirus disease 2019. J Traditi Chin Med 2020;61:655–9.
[13] Cheng DZ, Wang WJ, Li Y, Wu XD, Zhou B, Song QY. Analysis of 51 cases of novel coronavirus pneumonia treated with traditional Chinese medicine Lianhua Qingwen: a multicenter retrospective study. Tianjin J Tradit Chin Med. http://kns.cnki.net/kcms/detail/12.1349.R.20200310.1024.004.html.
[14] Yao KT, Liu MY, Li X, Huang JH, Cai HH. Retrospective Clinical Analysis on Treatment of Novel Coronavirus-infected Pneumonia with Traditional Chinese Medicine Lianhua Qingwen. Chinese Journal of Experimental Traditional Medical Formulae. http://kns.cnki.net/kcms/detail/11.3495.R.20200206.1500.004.html.
[15] Luo H, Tang QL, Shang YX, et al. Can Chinese medicine be used for prevention of corona virus disease 2019 (COVID-19)? A review of historical classics, research evidence and current prevention programs. Chin J Integr Med 2020;26:243–50.
[16] National Health Commission of the People's Republic of China. Transcript of the press conference on 17 February 2020. National Health Commission of the People's Republic of China, Beijing, 2020b.
[17] Zhu S, Li X, Wei Y. Preliminary study on the inhibition of SARS-associated coronavirus in three Chinese medicine prescriptions. Biotechnol Lett 2003;107:390–2.
[18] Chinese Academy of Military HospitalChinese academy of military medical sciences and Beijing Ditan hospital have confirmed anti-H1N1 influenza virus: Chinese medicine Lianhua Qingwen capsule has made a major breakthrough. J Chin Prescrip Drugs 2009;9:41.
[19] Ding Y, Zeng L, Li R, et al. The Chinese prescription Lianhua Qingwen capsule exerts anti-influenza activity through the inhibition of viral propagation and impacts immune function. BMC Complem. Altern M 2017;17:130.
[20] Duan Z, Jia Z, Zhang J, et al. Natural herbal medicine Lian hua qing wen capsule anti-influenza A (H1N1) trial: a randomized, double blind, positive controlled clinical trial. Chin Med J 2011; 124:2925–33.
[21] Mo H, Ke C, Zheng J, et al. Experimental study of Lianhua Qingwen capsule against influenza a virus in vitro. Tradit. Chin Drug Res Clin Pharmacol 2007;1:5–9.
[22] National Health Commission of the People's Republic of China. Guideline on diagnosis and treatment of SARS (2004 edition). National Health Commission of the People's Republic of China, Beijing, 2005.
[23] National Health Commission of the People's Republic of China. Guideline on diagnosis and treatment of MERS (2015 edition). National Health Commission of the People's Republic of China, Beijing, 2015.
[24] National Health Commission of the People's Republic of China. Guideline on diagnosis and treatment of Human Infection with H7N9 Avian Influenza (2017 edition). National Health Commission of the People's Republic of China, Beijing, 2017.
[25] National Health Commission of the People's Republic of China. Guideline on diagnosis and treatment of Influenza (2019 edition). National Health Commission of the People's Republic of China, Beijing, 2019.
[26] Li RF, Hou YL, Huang JC, et al. Lianhuaqingwen exerts anti-viral and anti-inflammatory activity against novel coronavirus (SARS-CoV-2). Pharmacol Res 2020;156:104761.
[27] Tang SW, Zhang YF, Liu KJ, et al. Effects of Lianhua Qingwen Capsule on lung tissue injury and expression of inflammatory cytokines in mice exposed to automobile exhaust. Chin J Exp Tradit Med Form 2015;13:139–43.
[28] Li Q, Yin J, Ran QS, et al. Efficacy and mechanism of Lianhua Qingwen Capsules (LHQW) on chemotaxis of macrophages in acute lung injury (ALI) animal model. Chin J Chin Mater Med 2019;44:2317–23.
[29] Ling XY, Tao JL, S X, et al. Exploring material basis and mechanism of Lianhua Qingwen Prescription against coronavirus based on network pharmacology. Chinese Traditional Herbal Drugs 2020;51:1723–30.
[30] Wang L, Yang ZH, Zhang HR, et al. Study on the network pharmacology and preliminary evidence of Lianhua Qingwen in the treatment of novel coronavirus (2019-nCoV) pneumonia. J Chin Med Materials 2020;43:772–8.
[31] Zhuang W, Fan Z, Chu Y, et al. (2020) Chinese patent medicines in the treatment of coronavirus disease 2019 (COVID-19) in China. Front Pharmacol 2020;11:1066.doi: 10.3389/fphar.2020.01066.