

The efficacy of different traditional Chinese medicine treatment for Corona Virus Disease 2019 : Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION**Support** - National Key Research and Development Program, 2021yfc1712901.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202430074**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 March 2024 and was last updated on 18 March 2024.**INTRODUCTION**

Review question / Objective Since the outbreak of the novel coronavirus pneumonia (COVID-19) epidemic at the end of 2019, based on the anti-epidemic experience of traditional Chinese medicine (TCM) experts, TCM treatment regimens represented by "three formulas and three medicines" have been widely used in clinical practice and have achieved good therapeutic effects. Currently, a large number of commonly used traditional Chinese patent medicines or prescriptions for upper respiratory tract infections are used in the treatment of COVID-19. Previous literature research has found that the drugs currently used clinically for the treatment of COVID-19 can be broadly divided into three categories. Which treatment method is the best? What are the advantages and disadvantages of each of the three methods?

Condition being studied COVID-19 is a respiratory infectious disease caused by infection with a novel coronavirus. Clinical symptoms often include fever, fatigue, cough, sputum production, muscle soreness, diarrhea, etc. Severe cases may experience respiratory distress and multiple organ failure. COVID-19 belongs to the category of "epidemic" and "plague" in TCM. Currently, there are no specific and effective targeted drugs for clinical treatment, with symptomatic treatment being the main approach. TCM has shown significant efficacy in the treatment of COVID-19, playing an important role in alleviating early discomfort symptoms in patients and reducing the rate of progression to severe cases. With the deepening understanding of the TCM diagnosis and treatment principles for COVID-19, although regional, climatic, and constitutional differences may lead to different manifestations of the disease, "dampness, toxin, stagnation, and

closure" are the main characteristics of COVID-19 pathogenesis. Stagnation of dampness and heat and closure of the lung by the epidemic toxin are the core pathogenesis of the disease, and clearing lung, detoxifying, expelling dampness, and promoting qi are the main treatment methods. Based on preliminary literature research, found that the drugs currently used in clinical practice for COVID-19 infection can be broadly categorized into three main types: one type is represented by commonly used drugs such as Shuanghuanglian and Jinhua Qinggan, which have the function of clearing lung and detoxification and are commonly used for influenza and other upper respiratory tract infections; another type of drugs is represented by Xuanfei Badu granules, which not only clear the lung and detoxify but also address the pathological manifestations of "dampness" in COVID-19, adding dampness-eliminating (dampness transforming, drying dampness, promoting diuresis) drugs (such as *Atractylodes*, *Pogostemonis Herba*, and *Sparganii Rhizoma*) on the basis of dispersing lung qi and detoxification; the third type of drugs is represented by Qingfei Paidu decoction and Ganlu Xiaodu decoction, which not only dispersing lung qi, detoxification, and eliminate dampness but also address the pathological manifestations of "dampness stagnating with heat" in COVID-19, adding qi-activating drugs (such as *Bupleuri Radix*, *Magnoliae Officinalis Cortex*, and *Arecae Semen*) on the basis of dispersing lung qi, detoxification and eliminating dampness.

METHODS

Search strategy The databases searched include CNKI, Wanfang Database, PubMed and Embase. The search period covered from the establishment of each database to April 5, 2023.

CNKI: (SU=(新型冠状病毒肺炎) OR SU=(新冠肺炎) OR SU=(2019新型冠状病毒感染疾病) OR SU=(2019新型冠状病毒感染) OR SU=(2019新冠肺炎) OR SU=(新型冠状病毒感染的肺炎) OR SU=(新型冠状病毒感染肺炎) OR SU=(2019新型冠状病毒感染肺炎) OR TKA=(新型冠状病毒肺炎)) AND (SU=(中药) OR SU=(中西医结合) OR SU=(中成药) OR SU=(草药) OR SU=(本草) OR SU=(生药) OR SU=(草本药) OR SU=(植物药) OR SU=(饮片) OR SU=(汤剂) OR SU=(丸剂) OR SU=(粉剂) OR SU=(膏方) OR SU=(民族药) OR SU=(民间方) OR SU=(注射液) OR SU=(注射剂) OR TKA=(中药) OR TKA=(中西医) OR TKA=(成药) OR TKA=(草药) OR TKA=(本草) OR TKA=(生药) OR TKA=(草本药) OR TKA=(植物药) OR TKA=(饮片) OR TKA=(汤) OR TKA=(丸) OR

TKA=(散) OR TKA=(膏) OR TKA=(民族药) OR TKA=(民间方) OR TKA=(注射液) OR TKA=(注射剂))

Wanfang: (主题:(新型冠状病毒肺炎) OR 主题:(新冠肺炎) OR 主题:(2019新型冠状病毒感染疾病) OR 主题:(2019新型冠状病毒感染) OR 主题:(2019新冠肺炎) OR 主题:(新型冠状病毒感染的肺炎) OR 主题:(新型冠状病毒感染肺炎) OR 主题:(2019新型冠状病毒感染肺炎) OR 题名或关键词:(新型冠状病毒肺炎) OR 摘要:(新型冠状病毒肺炎)) AND (主题:(中药) OR 题名或关键词:(中药) OR 摘要:(中药) OR 主题:(中西医) OR 题名或关键词:(中西医) OR 摘要:(中西医) OR 主题:(中成药) OR 题名或关键词:(中成药) OR 摘要:(成药) OR 主题:(草药) OR 题名或关键词:(草药) OR 摘要:(草药) OR 主题:(本草) OR 题名或关键词:(本草) OR 摘要:(本草) OR 主题:(生药) OR 题名或关键词:(生药) OR 摘要:(生药) OR 主题:(草本药) OR 题名或关键词:(草本药) OR 摘要:(草本药) OR 主题:(植物药) OR 题名或关键词:(植物药) OR 摘要:(植物药) OR 主题:(注射液) OR 题名或关键词:(注射液) OR 摘要:(注射液) OR 主题:(注射剂) OR 题名或关键词:(注射剂) OR 摘要:(注射剂))

Pubmed: (Medicine, Traditional[MeSH Terms]) OR (Medicine, Chinese traditional[MeSH Terms]) OR (Complementary Therapies[MeSH Terms]) OR (Plant Extracts[MeSH Terms]) OR (Drugs, Chinese Herbal[MeSH Terms]) OR (Herbal Medicine[MeSH Terms]) OR (Plants, Medicinal[MeSH Terms]) OR (Plant preparations[MeSH Terms]) OR (Medicine, Kampo[MeSH Terms]) OR (Phytotherapy[MeSH Terms]) OR (Chinese medicin*[Title/Abstract]) OR (Chinese herb*[Title/Abstract]) OR (Chinese plant*[Title/Abstract]) OR (Chinese drug*[Title/Abstract]) OR (Chinese formul*[Title/Abstract]) OR (Chinese prescri*[Title/Abstract]) OR (oriental medicin*[Title/Abstract]) OR (traditional medicin*[Title/Abstract]) OR (alternativ* medicin*[Title/Abstract]) OR (alternativ* therap*[Title/Abstract]) OR (complementary medicin*[Title/Abstract]) OR (complementary therap*[Title/Abstract]) OR (complementary treatment*[Title/Abstract]) OR (botanical extract*[Title/Abstract]) OR (plant extract*[Title/Abstract]) OR (plant preparation*[Title/Abstract]) OR (plant medicin*[Title/Abstract]) OR herb*[Title/Abstract] OR (herbal remed*[Title/Abstract]) OR (herbal extract*[Title/Abstract]) OR (herbal preparation*[Title/Abstract]) OR (herbal mixture*[Title/Abstract]) OR (herbal medicin*[Title/Abstract]) OR (phyto drug*[Title/Abstract]) OR (phyto pharmaceutical*[Title/Abstract]) OR (phyto therap*[Title/Abstract]) OR (phyto treatment*[Title/Abstract]) OR (phyto medicin*[Title/Abstract]) OR

(phytopharmaceutic*[Title/Abstract]) AND "COVID-19"[Mesh]

Embase: 'coronavirus disease 2019'/exp AND ('chinese medicine'/exp OR 'medicine, chinese traditional'/exp OR 'medicine, chinese traditional' OR 'complementary therapies'/exp OR 'complementary therapies' OR 'drugs, chinese herbal'/exp OR 'drugs, chinese herbal' OR 'chinese medicin*':ab,ti OR 'chinese herb*':ab,ti OR 'chinese plant*':ab,ti OR 'chinese drug*':ab,ti OR 'chinese formul*':ab,ti OR 'chinese prescri*':ab,ti OR 'oriental medicin*':ab,ti OR 'alternativ* medicin*':ab,ti OR 'alternativ* therap*':ab,ti OR 'complementary medicin*':ab,ti OR 'complementary therap*':ab,ti OR 'complementary treatment*':ab,ti).

Participant or population Patients diagnosed with COVID-19, without restrictions on age, gender, region, or classification, excluding suspected cases and cases in the recovery phase.

Intervention Intervention measures include traditional Chinese medicine therapy alone or combined with conventional Western medicine treatment. Traditional Chinese medicine formulations include but are not limited to decoctions, pills, granules, powders, ointments, and capsules.

Comparator Control measures include placebo, blank control, or conventional Western medicine treatment consistent with the experimental group. Conventional treatments include but are not limited to antiviral therapy, oxygen therapy, antibacterial drugs, and nutritional support.

Study designs to be included Study types are limited to randomized controlled trials (RCTs) and cohort studies.

Eligibility criteria Studies excluded are those involving animal experiments, with incorrect or incomplete data, unable to obtain the full text, or those that have been published repeatedly.

Information sources The electronic databases searched include CNKI, Wanfang Database, PubMed and Embase.

Main outcome(s) Nucleic acid conversion rate. The nucleic acid conversion rate refers to the proportion of individuals who initially tested positive (i.e., detected with viral nucleic acid) in a certain period of time, and subsequently tested negative (i.e., not detected with viral nucleic acid) in follow-up tests.

Additional outcome(s) Additional outcomes include chest CT recovery rate, rate of conversion to severe condition, time to nucleic acid conversion, time to chest CT recovery, length of hospital stay, and disappearance rate and time of corresponding symptoms (cough, sputum production, fatigue, muscle pain, shortness of breath, chest tightness, difficulty breathing, diarrhea, nausea, vomiting, poor appetite, dry throat, sore throat, headache, nasal congestion, runny nose).

Data management Two researchers independently conducted literature screening and data extraction, with discrepancies resolved by a third researcher. After importing the literature into Note Express software for plagiarism checking, the two researchers independently reviewed the titles and abstracts, conducting an initial screening of the retrieved literature. Subsequently, the literature included in the initial screening was read in full, and the final inclusion of literature was determined based on inclusion and exclusion criteria. Data extraction was performed using Excel software, including the following variables: article ID, age, gender, duration of illness, diagnostic criteria, classification of COVID-19, sample size, intervention and control measures (drug names, doses, intervention duration), outcome indicators, and results.

Quality assessment / Risk of bias analysis Two researchers independently conducted quality assessment of the literature and cross-checked their evaluations. In case of discrepancies, a third researcher assisted in resolving them. For randomized controlled trials, the Cochrane Handbook's Risk of Bias 1.0 tool was used for quality assessment. The assessment criteria covered the following five aspects: bias in the randomization process, bias in deviation from the intended intervention, bias in outcome measurement, bias in missing outcome data, and bias in selective outcome reporting. The Newcastle-Ottawa Scale (NOS) was used for quality assessment of cohort studies. Bias risk in the included studies was evaluated from three dimensions: selection of study participants, comparability between groups, and measurement of exposure factors.

Strategy of data synthesis The meta-analysis was conducted using RevMan 5.4.1 software. Relative risk (RR), odds ratio (OR), and their 95% confidence intervals (CIs) were used for analyzing count data in randomized controlled trials (RCTs) and cohort studies. Mean difference (MD) and its 95% CI were used for analyzing continuous data.

A significance level of $\alpha=0.05$ was applied, with $P<0.05$ indicating statistical significance. The heterogeneity among the data was assessed using the I² test, and a random-effects model was used for data analysis. Funnel plots were generated using R software, and Egger's test was conducted to evaluate publication bias.

Subgroup analysis We categorize the Chinese herbal medicine for treating COVID-19 into three subgroups based on their properties. Subgroup 1: "Dispersing lung qi and detoxification", Subgroup 2: "Dispersing lung qi, detoxification and eliminating dampness", and Subgroup 3: "Dispersing lung qi, detoxification, eliminating dampness and activating qi". We then analyzed the efficacy of these three Chinese herbal medicine treatments for COVID-19 across different outcome indicators.

Sensitivity analysis Sensitivity analysis will be performed on primary outcomes with excessive heterogeneity to explore the stability of the results.

Language restriction No restriction.

Country(ies) involved China.

Keywords Corona Virus Disease 2019; Promoting lung detoxification; Qi circulation; Turbid damp; Meta-analysis.

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