

The therapeutic efficacy of Xuanfei Baidu Formula combined with conventional drug in the treatment of coronavirus disease 2019

A protocol for systematic review and meta-analysis

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is a new acute respiratory infectious disease that has been in a public health emergency of international concern. In China, the combination of Xuanfei Baidu Formula (XBF) and conventional drug is used in the clinical treatment of patients with new coronary pneumonia. However, there is no comprehensive and systematic evidence on the effectiveness and safety of XBF.

Materials and Methods: We search for research in PubMed, China National Knowledge Infrastructure, Wan-fang Database, China Biomedical Database, and Chinese Science Citation Database. For “Xuanfei Baidu Formula” and “COVID-19,” we screened suitable articles without language restrictions on keywords. Review Manager 5.3 and STATA 14.2 software was used for the data analysis.

Results: The systematic review and meta-analysis will evaluate the efficacy and safety of XBF combined with conventional drug in the treatment of COVID-19.

Conclusion: We will provide evidence of XBF for the treatment on COVID-19 patients.

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Abbreviations: COVID-19 = corona virus disease 2019, XBF = Xuanfei Baidu formula.

Keywords: conventional drug, corona virus disease 2019, meta-analysis, protocol, systematic review, Xuanfei Baidu Formula

1. Introduction

Corona Virus Disease 2019 (COVID-19) is an RNA virus caused respiratory disease, which has posed an enormous threat to public health.^[1] Its long incubation period, strong contagiousness, the main transmission route is Respiratory droplet, also, it could be transmitted through person-to-person contacts by

asymptomatic carriers.^[2] According to statistics from the World Health Organization, as of Dec 3, 2020, This brings the cumulative numbers to over 61.8 million reported cases and 1.4 million deaths globally since the start of the pandemic.^[3] There is no effective way to control the COVID-19 and no vaccine is currently available.^[4] The treatment is only symptomatic. Therefore, the effective prevention and treatment of COVID-19 are a very urgent task.

Traditional Chinese medicine (TCM) has been proven effective for COVID-19 treatment.^[5] Xuanfei Baidu Formula was recommended as the treatment agent in the 8th edition of the "Diagnosis and Treatment Scheme for New Coronavirus Infected Pneumonia."^[6] Xiong Wuzhong et al recent study showed that Xuanfei Baidu Formula (XBF) is safe and effective for COVID-19 and can significantly improve COVID-19 patient's clinical symptoms, increase the number of white blood cells and lymphocytes to improve immunity, and also significantly reduce C-reactive protein and erythrocyte sedimentation rate to play an anti-inflammatory effect.^[7] Because of comprehensive and systematic evidence, we will collect all randomized controlled trials on XBF in the treatment of COVID-19, and present a meta-analysis protocol and systematic reviews.

2. Methods and program

The protocol has been registered on the International prospective register of systematic review (INPLASY), the registration number is INPLASY2020120011 (DOI: 10.37766/inplasy2020.12.0011).

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Because of no issues about participant privacy, the review will not require ethical approval.

The authors have no conflicts of interest to disclose.

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

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Table 1
PUBMED search strategy.

Number	Search terms
1	"randomized controlled trial" [Publication Type] OR "controlled clinical trial" [Publication Type] OR "Single-Blind Method" [Text Word] OR "random allocation" [Text Word] OR "RCT" [Text Word] OR "RCTs" [Text Word]
2	"Xuanfei Baidu Formula" [All Fields] OR "Xuanfei Baidu Decoction" [All Fields] OR "XuanfeiBaidu Formula" [All Fields] OR "XFB" [All Fields] OR "XFB Formula" [All Fields]
3	"COVID-19" [Title/Abstract] OR "coronavirus disease 2019" [Title/Abstract] OR "2019 novel coronavirus disease" [Title/Abstract] OR "2019-nCoV" [Title/Abstract] OR "SARSCov2" [Title/Abstract]
4	#1 AND #2 AND #3

The protocol followed Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) guidelines.^[8]

2.1. Literature search strategy

We search for research in PubMed, China National Knowledge Infrastructure, Wan-fang Database, China Biomedical Database, and Chinese Science Citation Database. Exemplary search strategy of PubMed is listed in Table 1. Full-text review was performed while the title/abstract thought to be thematic. The job above was executed by 2 investigators independently. The conflicts were resolved by consensus and discussion.

2.2. Inclusion criteria

2.2.1. Study design. The study trials were randomized controlled trials, participants age of 18 to 75 years old.

2.2.2. Diagnostic criteria. The specific IgM and IgG antibodies against SARS-COV-2 were positive in serum test.

2.2.3. Intervention group. The treatment group was given XBF on the basis of conventional drug treatment. Control group: only conventional drug treatment.

2.2.4. Main outcomes. Total efficacy, relief time of main symptoms(such as fever, cough, myalgia, or fatigue), relief time of

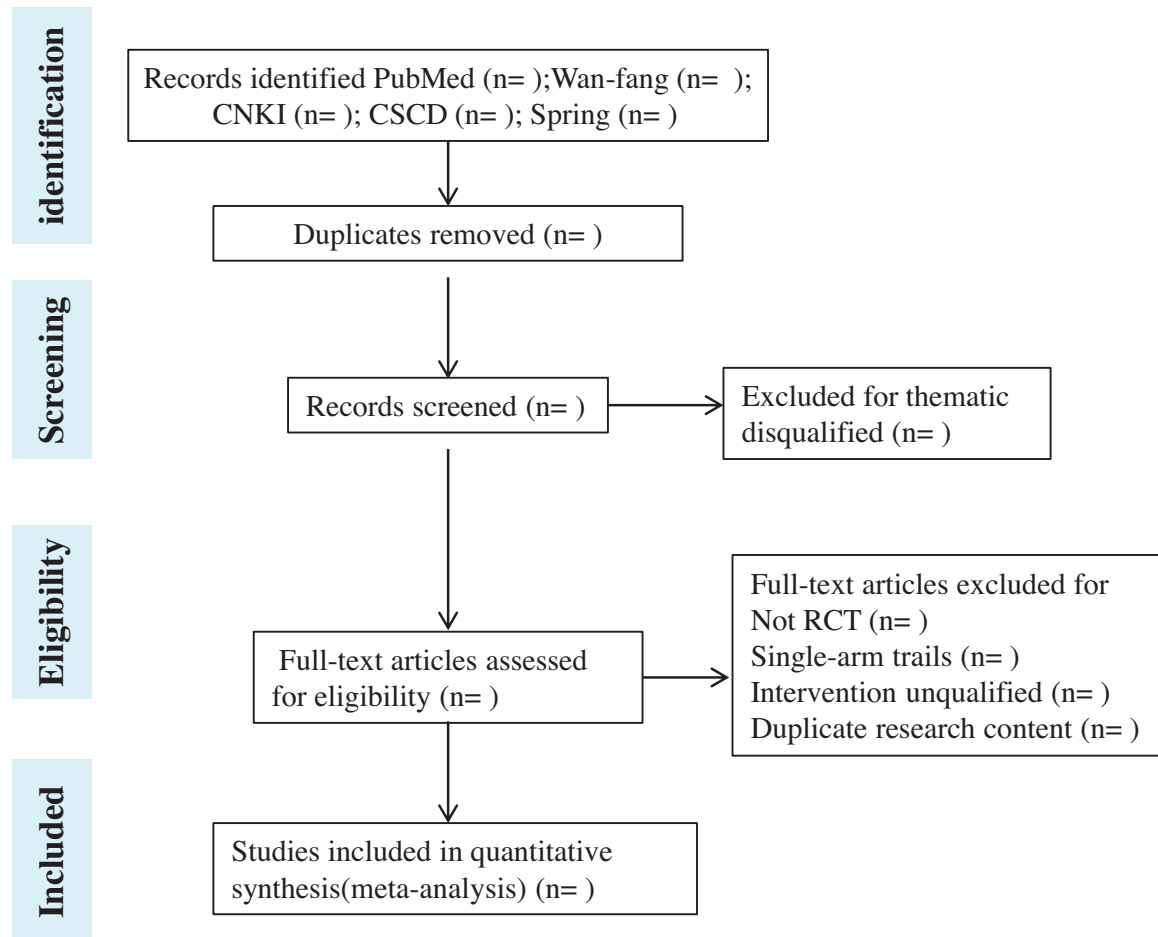


Figure 1. Process of study screening.

other symptoms (such as headache, dizziness, diarrhea, nausea and so on.) Additional outcomes: leukocyte, lymphocyte, C-reactive protein, adverse events.

2.3. Exclusion criteria

2.3.1 Some reviews, animal experiments, case report and comments et al. were thought to be unrelated with the topic.

2.3.2 Experiments without control or Diagnostic criteria statement was ambiguous.

2.3.3 The intervention of COVID-19 patients was not based on XBF treatment.

The full screening process is shown in PRISMA flow chart (Fig. 1).

2.4. Data extraction and quality assessment

Summarize the searched literatures, including basic characteristics, basic information, intervention measures, Outcome indicators. For example, author, publication time, number of samples in each group, age, ratio of male to female, drugs, time used in treatment, and so on. Then extracted data were assessed for Cochrane bias risk by 2 investigators independently.^[9] as follows: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias. Each term was judged with 3 levels—Low risk, High risk, Unclear risk” bias, If there are disagreements during the evaluation process, it will be resolved through discussion with a third investigator.

2.5. Data analysis

Data analysis was performed using Review Manager 5.3 (Cochrane Collaboration) and STATA 16.0 software. Outcome measures such as the total effective rate, the disappearance rate of main clinical features and the disappearance rate of minor symptoms were regarded as dichotomous variables and presented as the odds ratio (OR) with 95% confidence intervals (95% CI), and the risk ratio (OR) with 95% confidence intervals (95% CI). Contents of inflammatory cytokines were continuous variables that presented as the mean difference (MD) with 95% CI, Q statistic and I^2 tests were applied to assess the heterogeneity among studies.

When $I^2 \leq 25\%$, the data is considered homogeneous. A fixed-effects model was used to analyze data with low heterogeneity ($25\% \leq I^2 \leq 50\%$) and data with high heterogeneity ($P < .1$ or $I^2 > 50\%$) was estimated using random-effects model. Potential publication bias was revealed by funnel plots.^[10,11]

3. Discussion

We study to evaluate the clinical effect and safety of XBF on patients infected with COVID-19. With the advent of winter, many experts predict that the epidemic caused by COVID-19 will once again erupt globally.^[12,13] Traditional Chinese medicine has a history of more than 2000 years in the prevention and treatment of epidemics and plagues,^[14] In light of its experience treating SARS and H1N1 influenza, in the fight against COVID-19, China

achieved effect. Network pharmacology and molecular docking studies of XBF show that it has effect in the treatment of COVID-19 patients, by regulating key targets such as IL6, MAPK3, MAPK1, IL1 β , CCL2, EGFR.^[15] This study aims to evaluate the effectiveness and safety of XBF in the treatment of COVID-19, and to provide ways for the treatment of COVID-19.

Author contributions

Methodology: Fan Li.

Project administration: Fan Li.

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Supervision: Fang Li.

Visualization: Yajuan Li, Aj Mao.

Writing – original draft: Fan Li, Chongbo Zhao.

Writing – review & editing: Fang Li, Weifeng Wang

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