INPLASY PROTOCOL

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Conflicts of interest: None declared.

Effectiveness and Safety of Different Traditional Chinese Medicines for Coronavirus Disease 2019: A Systematic Review and Network Meta-analysis Protocol

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Review question / Objective: This study will provide evidence for the treatment of COVID-19 with TCM therapy, and provide ideas for the clinical treatment of COVID-19.

Condition being studied: All randomized controlled trials using traditional Chinese medicine to treat COVID-19 will be accepted. No language or publication status requirements. In addition, relevant non-randomized controls, reviews, individual cases, etc., were excluded.

Information sources: We will draw from 7 databases: PubMed, Cochrane Central Register of Controlled Trials, EMBASE, Web of Science, Chinese Biomedical Literature Database, Wanfang Database, The Chongqing VIP Database and Chinese National Knowledge Infrastructure were used to retrieve the randomized controlled studies on the treatment of 2019 Novel coronavirus pneumonia with Chinese medicine. The time limit was from the establishment of the Database to June 19, 2021. Meanwhile, We will also look for trials that have not yet been published in The ClinicalTrials.gov, Chinese Clinical Trial Registry.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 June 2021 and was last updated on 24 June 2021 (registration number INPLASY202160092).

INTRODUCTION

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METHODS

Participant or population: All randomized controlled trials using traditional Chinese medicine to treat COVID-19 will be accepted. No language or publication status requirements. In addition, relevant non-randomized controls, reviews, individual cases, etc., were excluded.

Intervention: The intervention measures of the experimental group were the treatment of COVID-19 with traditional Chinese medicine combined with or without western medicine, and the dose and frequency were not limited.

Comparator: The treatment of the control group could be TCM combined with western medicine or western medicine alone.

Study designs to be included: All randomized controlled trials using traditional Chinese medicine to treat COVID-19 will be accepted. No language or publication status requirements. In addition, relevant non-randomized controls, reviews, individual cases, etc., were excluded.

Eligibility criteria: High-quality methodological articles are critical to the credibility of the results, so we included only RCTs with a variety of drugs for urinalysis. Since all patients with end-stage uremia are undergoing hemodialysis, there is no requirement for hemodialysis mode and flux. On the basis of hemodialysis, combined with various drugs, drugs are only limited to Gabapentin, Pregabalin, Tacrolimus, and Ondancetron. The intervention measures of the control group should include placebo or blank control.

Information sources: We will draw from 7 databases: PubMed, Cochrane Central Register of Controlled Trials, EMBASE, Web of Science, Chinese Biomedical Literature Database, Wanfang Database, The Chongqing VIP Database and Chinese National Knowledge Infrastructure were used to retrieve the randomized controlled studies on the treatment of 2019 Novel

coronavirus pneumonia with Chinese medicine. The time limit was from the establishment of the Database to June 19, 2021. Meanwhile, We will also look for trials that have not yet been published in The ClinicalTrials.gov, Chinese Clinical Trial Registry.

Main outcome(s): 1. Cure rate. 2. Aggravation rate. 3. Mortality rate.

Additional outcome(s): 1. The negative conversion rate of nucleic acid test for SARS-CoV-19 2. Any adverse events.

Quality assessment / Risk of bias analysis: ject has three levels, high, low and undefined risk deviation levels. When relevant information is missing, we will email the author to obtain the original information. If the result is in dispute, the final result will be decided by the group discussion.

Strategy of data synthesis: Assessment of heterogeneity. Heterogeneity tests for all included studies were performed by using Network prediction interval graph, then to study the relationship of the weighted mean difference (WMD) at a 95% confidence interval (95% CI) and estimation zone (95%Prl) to invalid line, only when invalid line crosses perpendicularly to estimation zone but does not to CI, then it means that heterogeneity exists. If there is a direct comparison between the experimental interventions included in the data, the Stata14.0 will be used for pairwise meta-analysis based on a random-effects model. Network meta-analysis. Two team members (HB and SBC) used statistical software Stata (version 14.0; Stata Corporation, College Station, TX) for analysis. A random effects model was used for network meta-analysis to compare the variables between different interventions. By comparing Surface Under the Cumulative Ranking Curve (SUCRA), the optimum intervention measures were determined. The range of SUCRA is 0% to 100%; the higher of the cumulative ranking curve means the better of the efficacy.

Subgroup analysis: When there is obvious heterogeneity in the included articles, we will conduct subgroup analysis to reduce the heterogeneity, and analyze it from the aspects of drug dose, frequency, treatment course, etc.

Sensitivity analysis: We will exclude lowquality articles to test whether the conclusions of the meta-analysis are credible.

Country(ies) involved: China.

Keywords: COVID-19; network metaanalysis; protocol.

Contributions of each author:

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Author 3 - Chiheng Pi.

Author 4 - Shifan Yan.

Author 5 - Fusheng Li.