INPLASY PROTOCOL

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Review Stage at time of this submission: The review has not yet started.

Conflicts of interest: None.

Therapy of Diarrhea in COVID-19 with External Treatment of Traditional Chinese Medicine: a protocol for systematic review and meta analysis

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Review question / Objective: This meta-analysis of randomized controlled trials evaluated the effectiveness and safety of External Treatment of Traditional Chinese Medicine for diarrhea in COVID-19.

Condition being studied: From the end of 2019 to the present, COVID–19 has become a common problem worldwide now. At present, there is no effective antiviral drug confirmed by COVID-19. Diarrhea is common in patients with COVID-19. TCM has a unique theory and a long history of clinical practice. Due to its reliable efficacy and few side effects, it is widely used to treat diarrhea as one of TCM characteristic therapies. External treatment of traditional Chinese medicine includes acupuncture, moxibustion, massage, and acupoint application, acupoint embedding, etc. In China, External treatment of traditional Chinese medicine has been widely used in treating diarrhea in COVID-19, but there is still a lack of evidence-based medical evaluation.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 November 2020 and was last updated on 08 December 2020 (registration number INPLASY2020110095).

INTRODUCTION

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clinical practice. Due to its reliable efficacy and few side effects, it is widely used to treat diarrhea as one of TCM characteristic therapies. External treatment of traditional Chinese medicine includes acupuncture, moxibustion, massage, and acupoint application, acupoint embedding, etc. In China, External treatment of traditional Chinese medicine has been widely used in treating diarrhea in COVID-19, but there is still a lack of evidence-based medical evaluation.

METHODS

Participant or population: Patients diagnosed with COVID-19 and symptoms of diarrhea will be included regardless of sex, age, race, education, and economic status.

Intervention: Interventions will include the external treatment of traditional Chinese medicine. External treatment of traditional Chinese medicine will consist of acupuncture, massage, fire needle, moxibustion, etc. Other conventional Chinese therapies will be excluded.

Comparator: We will compare the following interventions: treatments other than traditional Chinese medicine (e.g., usual or standard care, placebo, wait-list controls).

Study designs to be included: All published randomized controlled trials in English or Chinese related to the external treatment of traditional Chinese medicine for diarrhea COVID-19 will be included.

Eligibility criteria: We will include articles related to traditional Chinese medicine's external treatment for treating COVID-19 patients with diarrhea. All included articles were randomized controlled trials. Due to language limitations, we will choose article published both in Chinese and English as long as it meets our inclusion criteria. Non-RCTs, quasi-RCTs, series of case reports, animal trials, and laboratory studies will be excluded.

Information sources: We plan to search the following Electronic databases: Cochrane Central Register of Controlled Trials, Embase, PubMed, Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Database (CBM), VIP database for Chinese technical Periodicals, and Wanfang Database.

Main outcome(s): Primary outcomes: Frequency of diarrhea and fecal texture. Compare the number of daily defecation and fecal texture before and after treatment. Secondary outcomes: Accompanying symptoms (such as myalgia, expectoration, stuffiness, runny nose, pharyngalgia, anhelation, chest distress, dyspnea, crackles, headache, nausea, vomiting, anorexia, diarrhea) disappear rate, negative COVID-19 results rate on two consecutive occasions (not on the same day), CT image improvement, average hospitalization time, the occurrence rate of common type to a severe form, clinical cure rate, and mortality.

Quality assessment / Risk of bias analysis: We will evaluate all the included studies according to the Cochrane Handbook guidelines for Systematic Reviews of Interventions. Two researchers would independently assess the evaluation above. Any discrepancies will be resolved by consensus or by a discussion with a third reviewer. Evaluation items contain the following seven items: random sequence generation, allocation concealment, outcome evaluators, blinding of participants and personnel, incomplete outcome data, selective reporting, and other bias sources. The studies' risk of bias will be divided into three levels (low risk, high risk, and unclear).

Strategy of data synthesis: We will use Review Manager 5.3 and STATA 15.1 software for meta-analysis. The I2 test will be used to detect heterogeneity between trials. When the I2test value> 50%, there is significant statistical heterogeneity, and we will use a random-effects model. When the I2test value is less than or equal to 50% and no statistical heterogeneity is found, the fixed effects model is used for data synthesis. All participants will discuss possible causes from a clinical and

methodological perspective and provide descriptive or subgroup analysis.

Subgroup analysis: If possible, a subgroup analysis will be performed to explain the reasons for the heterogeneity. Factors such as different types of control interventions and different outcomes will be considered.

Sensibility analysis: If there is apparent heterogeneity in the tests included after the subgroup analysis, we will conduct a sensitivity analysis based on sample size, research design, heterogeneous quality, methodological quality, and statistical model to exclude quality Defect tests to ensure the analysis results' stability.

Language: The language is limited to Chinese and English.

Country(ies) involved: China.

Keywords: COVID-19; Traditional Chinese Medicine; diarrhea; protocol; systematic review.

Contributions of each author:
Author 1 - Cheng Cheng - drafted the manuscript.
Author 2 - Yashuang Huang - extracted the data.
Author 3 - Li Xie - extracted the data.
Author 4 - Xinghui Zhu - extracted the data.
Author 5 - Dongmei Chen - extracted the data.
Author 6 - Cisong Cheng - Writing - review & editing.