

Traditional Chinese Medicine Decoction for Acute Pancreatitis in Elderly Patients: A Protocol for Systematic Review and Network Meta-analysis

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Abstract: Background Acute pancreatitis is the most common disease of the pancreas, and is a common cause of acute abdominal pain. Elderly patients with acute pancreatitis are more likely to develop complications, and they experience substantially higher mortality than the middle-aged patients. Although many studies have shown that traditional Chinese medicine are effective for the treatment of acute pancreatitis, the efficacy and safety of different traditional Chinese medicine decoctions for acute pancreatitis in elderly patients are not fully clarified. In addition, because many traditional Chinese medicine decoctions are available for the pancreatitis, the selection of an appropriate decoction has become a pressing issue. This study aimed to compare the effectiveness of different traditional Chinese medicine decoction for elderly patients with acute pancreatitis by using network meta-analysis. Methods Random clinical studies on traditional Chinese medicine decoction for acute pancreatitis will be searched using the following databases: PubMed, Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, Wan Fang Database, VIP Database for Chinese Technical Periodicals, Medline, and Clinical Trial Register, from their inception to June 2022. Network meta-analyses will be performed to examine the efficacy of different traditional Chinese medicine decoction in the treatment of acute pancreatitis. Results This study will evaluate the effectiveness of different traditional Chinese medicine decoction in elderly patients with acute pancreatitis. Conclusion Results from this study may contribute to provide evidence for selecting an appropriate traditional Chinese medicine decoction for elderly patients with acute pancreatitis.

Keywords: Traditional Chinese medicine decoction, Acute pancreatitis, Elderly patients, Protocol, Network meta-analysis.

1. Introduction

Acute pancreatitis (AP) is a common cause of acute abdomen and a leading cause of hospitalization [1]. The estimated incidence of AP is approximately 34 per 100000 people worldwide, and the case fatality rate ranges from 15 to 30% [2]. Epidemiological studies and systematic reviews have shown that the incidence of AP is increasing globally [2-3]. Based on the revised Atlanta Classification (RAC), The severity of AP is generally classified as mild, moderately severe, and severe. 80%-85% of AP cases are classified as mild and 15%-20% as moderate or severe. [4]. Although most APs are mild, the mortality rate of severe pancreatitis can be as high as 30% [5]. The common causes of AP are biliary disease, hypertriglyceridaemia (HTG), alcohol consumption and endoscopic retrograde cholangiopancreatography (ERCP) [6]. These etiologies reported similar mortality rates [6-7]. Elderly AP patients are more susceptible to develop complications [8]. A retrospective comparative study comparing the epidemiology and outcomes between elderly and young-aged patients with AP showed that elderly patients had a higher proportion of multiple organ dysfunction syndrome (MODS), systemic inflammatory reaction syndrome, and shock. The mortality rate in the elderly patients was 1.69%, while that in the young and middle-aged patients was only 0.72%. Therefore, it is necessary to determine appropriate strategies for the treatment and prevention of AP in elderly patients.

Traditional Chinese medicine (TCM) has been successfully used to treat AP for several years. Numerous systematic

reviews, meta-analyses and prospective studies have confirmed that proprietary Chinese medicines can significantly improve clinical symptoms and potentially ameliorate disease progression [9]. The TCM decoction commonly used in the treatment of AP includes the Dachaihu and Dachengqi decoctions. Clinical evidence suggests that TCM decoctions can significantly improve clinical symptoms and potentially ameliorate disease progression [10]. TCM decoctions are recommended by guidelines as they improve symptom burden and contribute to the rapid recovery of gastrointestinal function [11]. Although there are many types of TCM decoction in clinical applications, there is little evidence comparing the clinical efficacy of a variety of TCM decoction in elderly AP patients.

As a statistical method to compare the effects of two or more treatments and allow ranking of different treatments, network meta-analysis (NMA) has the advantage of making comparisons of specific interventions that have not been compared directly head-to-head. Therefore, the purpose of this study was to evaluate the effectiveness and safety of different TCM decoction in elderly patients with AP using NMA and to contribute to clinical decision-making in treatment.

2. Methods

The systematic review and NMA will be performed following the guidelines of the Preferred Reporting Items for Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2015[12].

2.1. Registration Number

This protocol has been registered on the International Platform. (INPLASY202270119 <https://inplasy.com/inplasy-2022-7-0119/>).

2.2. Inclusion Criteria

Randomized controlled trial (RCT) studies meeting the criteria of PICOS (population, intervention, comparison, outcome, and study type)

1. Participants: Patients aged 60 years or older, with a confirmed diagnosis of AP.

2. Interventions: The experimental group was treated with a TCM decoction alone or in combination with other conventional Western medicine. The use of TCM decoction is limited to oral administration..

3. Comparators: The control group was treated with conventional Western medicine recommended by internationally authorized clinical guidelines or a placebo.

4. Outcome:

The primary outcomes: effectiveness rate, VAS scores for abdominal pain, VAS scores for nausea/vomiting, and time to first defecation.

The secondary outcomes: serum amylase level, mortality, and adverse reactions.

5. Type of study: RCTs about the effects of TCM decoction for AP, regardless of blinding or allocation concealment.

2.3. Exclusion Criteria

1. The experimental group patients was treated with TCM decoction combined with acupuncture, moxibustion, or other TCM methods.

2. Accurate data are not available.

3. Studies with inconsistent scoring criterias.

2.4. Retrieval Strategy

Two researchers will independently screen the literature and extracted data from Web of Science, PubMed, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), VIP Database, Wan Fang Database (Wan Fang), Chinese Biomedical Literature Database (CBM), Medline, and Clinical Trial Register (CTR). We will search the databases from the time of their inception to November 2021. The retrieval strategy differs according to different databases. The literature search also included gray documents such as conference papers and dissertations.

A combination of medical subject words and keywords, such as "Traditional Chinese Medicine" and "acute pancreatitis" will be used. Table 1 presents the search strategy using PubMed as an example.

2.5. Studies Selection

Duplicate literature will be excluded from the study using the NoteExpress 3.2.0. Two researchers independently will screen the literature and read the article titles and abstracts. After preliminary screening, the full texts of the articles will be checked to determine whether they should be included in the study. In case of differences, the issue will be addressed through intervention by a third researcher. A flowchart of the identification process is shown in Figure 1.

2.6. Data Extraction

Two researchers independently will extract the following data: title, first author, publication date, journal, registration number, inclusion criteria, diagnostic criteria, disease severity

(mild, moderately severe, or severe), sample size, randomization, blinding, treatment, interventions, adverse reaction events, and outcome indicators. Data will be checked after extraction and any disagreement was addressed through discussion with a third researcher.

2.7. Statistical Analysis

Stata software (version 14.0) and Markov chain–Monte Carlo method will be used to conduct the Bayesian meta-analysis. We will introduce three Markov chains in the simulation. The number of iterations will be set to 50,000 (the first 20,000 were used for annealing to eliminate the effect of the initial value, and the last 30,000 were used for sampling) [13].

The reticular diagram will be drawn the Stata 15.0 software. The consistency of each closed loop will be evaluated by relative odds ratios (OR) and 95% confidence intervals (CI). If the relative OR is close to 1, the fixed effects model will be adopted for analysis. Otherwise, the closed loop is considered to have obvious inconsistencies, and the random effects model will be used for analysis. Ranking interventions will be implemented by WinBUGS 1.4.3. [13].

2.8. Subgroup Analysis

Because different degrees of disease severity have been shown to have different prognoses, subgroup analysis will be classified according to disease severity (mild, moderately severe, or severe). In cases of significant heterogeneity among the included studies, a subgroup analysis will be performed based on the type of TCM decoction or other factors.

2.9. Assessment of Publication Bias

We will assess the risk of bias using the Cochrane Risk of Bias Tool. Two independent reviewers will assess seven items, including the allocation concealment, blinding of participants' personnel, risk of bias in sequence generation, outcome assessment, incomplete outcome data, selective outcome reporting, and other biases. The risk of bias will be judged to be low, high, or unclear.

2.10. Managing Missing Data

If missing data or reports lacked information, the corresponding authors of the articles will be contacted to obtain the relevant information.

2.11. Sensitivity Analysis

Sensitivity analysis will be conducted by excluding each study.

2.12. Assessment of the Quality of Evidence

The grading of recommendation assessment, development, and evaluation reliability will be implemented to assess the quality of evidence. Based on bias, inconsistency, inaccuracy, indirect bias, and the risk of publication bias. The evidence will be divided into high, medium, low, and very low levels.

2.13. Ethics

As no information was obtained from individual participants, the systematic review did not require ethical approval.

3. Discussion

AP is a common cause of acute abdomen, with a case

fatality rate ranging from 15 to 30%. Elderly patients with AP are likely to be more susceptible to complications, and disease severity and mortality are higher than in young and middle-aged patients. Studies have shown that proprietary TCM decoctions can significantly improve clinical symptoms and potentially ameliorate disease progression [14-16]. Therefore, this study aimed to evaluate the advantages and disadvantages of various TCM decoctions for the treatment of elderly patients with AP using the NMA method. The quality of the analysis may have depended on the quality and validity of the individual studies included. Due to the diversity of clinical medications, we could not include all categories of TCM decoction, which may increase the potential risk for bias in relevant studies. We hope that our research will be beneficial to clinicians and patients in selecting treatment strategies.

4. Author Contributions

Conceptualization: Yong Wang, Ying Sun

Data curation: Yong Wang, Ying Sun, Canzheng Wei.

Formal analysis: Yong Wang, Ying Sun, Hong Mu.

Methodology: Yong Wang, Hong Mu, Canzheng Wei.

Software: Yong Wang, Ying Sun.

Supervision: Yong Wang, Tengting Chang, Hong Mu, Ping

Li

Writing – original draft: Yong Wang

Writing – review & editing: Ying Sun, Tengting Chang,

Hong Mu.

The guarantor of the review: Ying Sun

5. List of Abbreviations

TCM = Traditional Chinese medicine.

RCT = random clinical research.

AP = Acute pancreatitis.

RAC = Revised Atlanta Classification

HTG = hypertriglyceridaemia

ERCP = endoscopic retrograde cholangiopancreatography

Footnotes

As no information was obtained from individual participants, the systematic review did not require ethical approval.

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The datasets used in this study are available from the corresponding authors upon request.

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