

# INPLASY PROTOCOL

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**Review Stage at time of this submission:** Formal screening of search results against eligibility criteria.

**Conflicts of interest:**  
None.

## Efficacy and safety analysis of Chinese herb injections promoting blood circulation combined with intravenous thrombolysis with alteplase in hyperacute cerebral infarction patients: a systematic review and meta-analysis

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**Review question / Objective:** **P:** This study will include patients who were diagnosed as hyperacute cerebral infarction(HCI) regardless their race, gender, and age. **I:** In the intervention group, all eligible HCI patients received Chinese herb injections promoting blood circulation combined with intravenous thrombolysis with alteplase. **C:** In the control group, all included HCI participants underwent intravenous thrombolysis with alteplase. **O:** The primary outcome is total clinical efficiency based on NIHSS score. The secondary outcomes include NIHSS score, cerebral infarction volume, serum biochemical index, hemorheology index, coagulation function, quality of life, and any untoward effects.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 June 2020 and was last updated on 24 June 2020 (registration number INPLASY202060093).

### INTRODUCTION

**Review question / Objective:** **P:** This study will include patients who were diagnosed

as hyperacute cerebral infarction(HCI) regardless their race, gender, and age. **I:** In the intervention group, all eligible HCI patients received Chinese herb injections

promoting blood circulation combined with intravenous thrombolysis with alteplase. C: In the control group, all included HCl participants underwent intravenous thrombolysis with alteplase. O: The primary outcome is total clinical efficiency based on NIHSS score. The secondary outcomes include NIHSS score, cerebral infarction volume, serum biochemical index, hemorheology index, coagulation function, quality of life, and any untoward effects.

**Condition being studied:** Acute cerebral infarction (ACI) is the most common type of stroke in China, accounting for 69.6%~70.8% of stroke. Its mortality rate is 14.4%~15.4%, and the disability rate is 33.4%~33.8%. Hyperacute cerebral infarction (HCl) refers to cerebral infarction within 6 hours of onset. Some studies have shown that the main mechanism of the Chinese herb injections promoting blood circulation (CHIPBC) of acute ischemic stroke is to improve hemorheology, ameliorate hemodynamics, improve microcirculation, promote blood vessel regeneration, improve ischemic reperfusion injury and so on. In recent years, the clinical study on the treatment of hyperacute cerebral infarction(HCl) with the combination of CHIPBC combined with intravenous thrombolysis with alteplase has been increasing gradually in China, but no systematic review of such clinical research has been found. Therefore, the purpose of this study is to systematically evaluate the efficacy and safety of CHIPBC combined with intravenous thrombolysis with alteplase in the treatment of HCl, and to provide reference for its safe and rational use in clinical practice.

## METHODS

**Participant or population:** Patients who were diagnosed as hyperacute cerebral infarction(HCl) regardless their race, gender, and age.

**Intervention:** Chinese herb injections promoting blood circulation combined with intravenous thrombolysis with alteplase.

**Comparator:** Intravenous thrombolysis with alteplase.

**Study designs to be included:** Randomized controlled trials,(RCTs), whether blind or not.

**Eligibility criteria:** For the included trials, the investigators need to precisely report the stochastic methods, Chinese herb injections promoting blood circulation treatment details and parameters, diagnostic criteria and efficacy evaluation they based on. Baseline assessments were necessary. Only randomized controlled studies were included. No limitation to whether it is published or not. The experiment is limited to humans. Language is limited to Chinese and English.

**Information sources:** A comprehensive search of 7 medical databases, including PubMed, Cochrane Library, Clinical Trails, China National Knowledge Infrastructure (CNKI), Chinese Scientific Journals Database (VIP), Wanfang Database and Chinese Biomedical Literature Database (Sino Med) from 2000 to April 2020. The language is restricted to Chinese and English. All literature reviews were performed by two independent researchers.

**Main outcome(s):** The main outcomes are clinical efficacy of neurological deficit and improvement of neurological function based on NIHSS score.

**Quality assessment / Risk of bias analysis:** Two investigators will independently evaluate the methodological quality of the included literature by using the Cochrane Collaboration's risk of bias assessment tool which includes 7 items: 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), other bias. According to the relevant standards in the Cochrane Intervention System Evaluation Manual, it will be divided into low risk, high

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risk and unclear. Any disagreements were resolved by discussion.

**Strategy of data synthesis:** Data were analyzed using RevMan 5.4. Dichotomous data will be expressed as the risk ratio (RR), and continuous outcomes will be presented as the mean difference (MD). 95% confidence intervals (95% CI) will be calculated for both types of data. A Cochran's Q-test with  $P > 0.10$  and an  $I^2$  of no more than 50% indicated that statistical homogeneity was acceptable. When the heterogeneity exists ( $I^2 > 50\%$  or  $P < 0.1$ ), random effects model was applied to estimate the data synthesis, otherwise a fixed effects model for meta-analysis was used. Descriptive analysis will be performed on data that cannot be synthesized.

**Subgroup analysis:** Data permitting, we will perform subgroup analysis considering different study characteristics, patient characteristics, and outcome measurements.

**Sensitivity analysis:** We will exclude each study which is included in the analysis, reanalyze and pooled the data, then compare the difference between the reobtained effects and the original effects. In this way, we will be able to assess the impact of individual studies on the overall results and whether the results are credible.

**Language:** English and Chinese.

**Country(ies) involved:** China.

**Keywords:** Chinese herb injection; Promoting blood circulation; Intravenous thrombolysis; Alteplase; Hyperacute cerebral infarction; Meta-analysis; Systematic review.

**Dissemination plans:** We will submit this study to a peer-reviewed journal for publication.

**Contributions of each author:**

Author 1 - Shanshan Gao - Shanshan Gao (GSS) initiated the study and participated in

the design, database search, study selection, data extraction, quality assessment; statistical analysis and drafted the manuscript.

Author 2 - Dongdong Yang - Dongdong Yang (YDD) developed the research design and supervised all aspects of the study.

Author 3 - Hengni Yan - Hengni Yan (YHN) helped to search databases, study selection, data extraction and quality assessment.

Author 4 - Yuxuan Chao - Yuxuan Chao (CYX) participated in statistical analysis and quality assessment.

Author 5 - Yu Fang - Yu Fang (FY) participated in search strategy.