## INPLASY PROTOCOL

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Conflicts of interest: None declared. Efficacy and Safety of Various Traditional Chinese Medicine Injections for Posterior Circulation Ischemia (PCI): A Protocol for Systematic Review and Network Meta-analysis

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**Review question / Objective:** The purpose of this study is to conduct a network meta-analysis to assess the benefits of Chinese Herbal injections (CHI) to treat Posterior Circulation Ischemia (PCI).

Condition being studied: The posterior circulation, also known as the vertebrobasilar system, consists of the vertebral artery, the basilar artery, and the posterior cerebral artery. Posterior Circulation Ischemia (PCI) is a common ischemic cerebrovascular disease, accounting for approximately 20% of ischemic strokes. Common symptoms of PCI include dizziness or vertigo, numbness of the limbs or head and face, weakness of the limbs, headache, vomiting, diplopia, transient loss of consciousness, visual disturbances, unsteadiness in walking or falling. Posterior circulation ischemic vertigo is often a precursor to stroke onset and is likely to lead to posterior circulation cerebral infarction, which can be lifethreatening in severe cases. The incidence of Posterior Circulation Ischemia (PCI) is high and the current optimal time window for thrombolytic therapy is short. Chinese Herbal injections (CHI) have better efficacy for the treatment of PCI.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 June 2022 and was last updated on 20 June 2022 (registration number INPLASY202260082).

## INTRODUCTION

**Review question / Objective:** The purpose of this study is to conduct a network metaanalysis to assess the benefits of Chinese Herbal injections (CHI) to treat Posterior Circulation Ischemia (PCI). Condition being studied: The posterior circulation, also known as the vertebrobasilar system, consists of the vertebral artery, the basilar artery, and the posterior cerebral artery. Posterior Circulation Ischemia (PCI) is a common ischemic cerebrovascular disease, accounting for approximately 20% of ischemic strokes. Common symptoms of PCI include dizziness or vertigo, numbness of the limbs or head and face, weakness of the limbs, headache, vomiting, diplopia, transient loss of consciousness, visual disturbances, unsteadiness in walking or falling. Posterior circulation ischemic vertigo is often a precursor to stroke onset and is likely to lead to posterior circulation cerebral infarction, which can be lifethreatening in severe cases. The incidence of Posterior Circulation Ischemia (PCI) is high and the current optimal time window for thrombolytic therapy is short. Chinese Herbal injections (CHI) have better efficacy for the treatment of PCI.

## **METHODS**

Participant or population: Patients should meet the diagnostic criteria for posterior circulation ischemic vertigo in the 2006 "Expert Consensus on Posterior Circulation Ischemia in China" or the 1989 "Possible Vertebrobasilar Artery Insufficiency" recommended by the World Health Organization (WHO).

Intervention: The intervention group was treated with Chinese herbal injection alone or with conventional treatment with herbal injection combined with western medicine.

**Comparator:** Thrombolytic, antiplatelet, anticoagulation and nutritional nerve therapy and control of blood pressure, blood glucose, and blood lipids will be considered as routine treatments.

Study designs to be included: Randomized controlled trails (RCT).

**Eligibility criteria:** Reported in P.I.C.O.S. items.

Information sources: Two authors will extract the data independently from the electronic databases such as PubMed. Any disagreements will be resolved through discussion until consensus is reached or a third author is consulted. The following data will be extracted: authors, year of publication, country in which the study was conducted, initial inclusion criteria, total number of people included in the study, interventions, duration of treatment, and outcome indicators.

Main outcome(s): Vertebrobasilar artery mean blood flow velocity.

Additional outcome(s): Changes in blood rheological indices before and after treatment. Changes in blood lipid indicators. Changes in TCM evidence score.

Quality assessment / Risk of bias analysis: Two reviewers will independently assesses the quality of the selected studies according to the Cochrane Collaboration's tool for randomized controlled trials Items will be evaluated in three categories: Low risk of bias, unclear bias and high risk of bias. The following characteristics will be evaluated: Random sequence generation(selection Bias) Allocation concealment(selection bias)Blinding of participants and personnel (performance bias)Incomplete outcome data (attrition bias) Selective reporting(reporting bias). Other biases Results from these questions will be graphed and assessed using Review Manager 5.4.

Strategy of data synthesis: Direct comparisons of CHI efficacy will be performed using Review Manager 5.3. The outcomes will be mainly represented by the mean difference or odds ratio with 95% confidence intervals, and a P value<.05 will be considered significant. The Cochrane Q test and I2 statistics were used to assess heterogeneity. When P 50%, which indicates statistical heterogeneity, a random-effects model will be used to calculate the outcomes; otherwise, a fixedeffects model will be considered. A network evidence diagram will be drawn to visually represent the comparisons between the studies. The size of the nodes represents the number of participants, and the thickness of the edges represents the number of comparisons. Stata 14.2 and WinBUGS 1.4.3 Software will be used to carry out Bayesian network meta-analysis. Bayesian inference will carried out using the Markov chain Monte Carlo method, the

posterior probability will be inferred from the prior probability, and estimation and inference will be assumed when Markov Chain Monte Carlo reaches a stable convergence state. As a result, the rank of the CHI effect will be presented by the surface under the cumulative ranking curve.

Subgroup analysis: If necessary, we will differentiate subgroups according to the severity of the disease.

Sensitivity analysis: To ensure robustness of the combined results, sensitivity analyses will be performed to assess the impact of studies with a high risk of bias. We will compare the results to determine whether lower-quality studies should be excluded.

Country(ies) involved: China.

Keywords: Posterior Circulation Ischemia, Chinese herbal injection, network metaanalysis.

Contributions of each author: Author 1 - Zunhao Tang.

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- Author 3 Hongshuo Shi.
- Author 4 Dong Guo.