INPLASY PROTOCOL

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The authors have no conflicts of interest to declare.

The efficacy of herbal medicines for acute ischemic stroke: A systematic review and network meta-analysis

Song, J[1]; Kim, H[2].

Review question / Objective: **Are herbal medicines effective in improving neurological outcomes in patients with acute ischemic stroke? Which herbal medicines have the most beneficial effects in acute ischemic stroke?**
Condition being studied: **Ischemic stroke occurs when a vessel supplying blood to the brain is obstructed, and induces long-term disability including motor, sensory, and cognitive deficits. It accounts for approximately 80 to 90 percent of all strokes.**
Information sources: **The following electronic databases will be searched: MEDLINE; EMBASE; Cochrane Library; Web of Science; Chinese National Knowledge Infrastructure (CNKI); National Digital Science Library (NDSL); and Korean Medical Article Database (KMbase).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 May 2020 and was last updated on 17 May 2020 (registration number INPLASY202050070).

INTRODUCTION

Review question / Objective: **Are herbal medicines effective in improving neurological outcomes in patients with acute ischemic stroke? Which herbal medicines have the most beneficial effects in acute ischemic stroke?**

Condition being studied: **Ischemic stroke occurs when a vessel supplying blood to the brain is obstructed, and induces long-term disability including motor, sensory,**

and cognitive deficits. It accounts for approximately 80 to 90 percent of all strokes.

METHODS

Participant or population: Participants who were diagnosed with acute ischemic stroke by computerized tomography (CT) or magnetic resonance imaging (MRI) regardless of their sex, age or race were eligible.

Intervention: All types of herbal medicines will be included, including single and multiple herbal medicines. There are no limitations on the administration routes, dosage, and duration of treatments.

Comparator: Randomized controlled trials where the control group received the placebo, no intervention, or drugs will be included. Co-intervention (conventional medicine) will also be allowed if applied in all arms. Trials that have assessed the combined effects of herbal medicines with other interventions, such as acupuncture, will be excluded, as the therapeutic effects of herbal medicines may not be distinguishable from the effects of other interventions. In addition, studies where the control group received non-conventional medicine will be excluded.

Study designs to be included: This study will include randomized controlled trials of herbal medicines for the treatment of acute ischemic stroke.

Eligibility criteria: Only randomized controlled trials of herbal medicines for the treatment of acute ischemic stroke will be included. There will be no restrictions regarding language or publication status. Non-randomized trials, case reports, observational studies, and reviews will be excluded.

Information sources: The following electronic databases will be searched: MEDLINE; EMBASE; Cochrane Library; Web of Science; Chinese National Knowledge Infrastructure (CNKI); National Digital Science Library (NDSL); and Korean Medical Article Database (KMbase).

Main outcome(s): Change in neurological impairment from baseline to the last available follow-up, measured using global outcome measures (e.g., National Institutes of Health Stroke Scale and modified Rankin scale).

Quality assessment / Risk of bias analysis: Two researchers will independently assess the risk of bias for each trial using the Cochrane risk of bias tool provided by Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0, Mar 2011). The following categories of bias will be assessed: selection bias (sequence generation and allocation concealment); performance bias (blinding of participants and personnel); detection bias (blinding of outcome assessment); attrition bias (incomplete outcome data); reporting bias (selective outcome reporting); and other bias (imbalance of the baseline information). Each domain will be graded as low risk, high risk, or unclear risk. Disagreements will be resolved by discussion with the third researcher.

Strategy of data synthesis: Data synthesis will be performed by using RevMan Review Manager Software (version 5.3). We will perform a pairwise meta-analysis using a random-effects model. To determine the effect size, risk ratios with 95% confidence intervals will be calculated for dichotomous outcomes and the standard mean differences with 95% confidence intervals will be calculated for continuous outcomes. Depending on the heterogeneity assessed by the I^2 statistic, a fixed- or random-effect model will be used. If there is statistical heterogeneity, sensitivity or subgroup analysis will be performed to explore the source of heterogeneity. We will then perform a Bayesian network meta-analysis using a random-effects model to analyze pooled data for different interventions.

Subgroup analysis: We plan to perform subgroup analyses for different groups split by severity of ischemic stroke, duration of treatment, or types of outcome measures.

Sensibility analysis: If sufficient data are extracted, a sensitivity analysis will be conducted to check the robustness of the results by excluding studies with low methodological quality.

Country(ies) involved: Republic of Korea.

Keywords: Stroke; herbal medicine; herb; systematic review; meta-analysis.

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