INPLASY PROTOCOL

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Conflicts of interest:
None.

Effects of danhong injection for cerebral infarction A protocol for systematic review and meta-analysis

Pan, P[1]; Zhao, Y[2]; Wang, J[3].

Review question / Objective: **Cerebral infarction (CI), also known as ischemic stroke, refers to the disorder of cerebral blood supply caused by various reasons, resulting in irreversible damage to local brain tissue, leading to ischemic anoxic necrosis of brain tissue, and then showing the corresponding neurological damage. Its high morbidity, high disability rate and high mortality rate have become public health issues of global concern. The main clinical manifestations of the patients were loss of self-care ability, speech disorder, hemiplegia, mental retardation and so on, which increased the social and family burden. Therefore, the effective treatment of cerebral infarction is of great significance to reduce the severity of cerebral infarction. Danhong injection is refined from Salvia miltiorrhiza and Carthamus tinctorius, which has the effect of promoting blood circulation and removing blood stasis, dredging pulse and relaxing meridians and collaterals. It has been found that Danhong injection has a neuroprotective effect on cerebral ischemia-reperfusion injury and is effective in the recovery of stroke. Danhong injection can significantly reduce the activities of monoamine oxidase and malondialdehyde in brain tissue, increase the activity of superoxide dismutase, improve hemorheology and serum NO content, and promote angiogenesis. Although a large number of studies have shown that Danhong has a good clinical effect on cerebral infarction. At present, there is no comprehensive and systematic evidence to confirm its clinical efficacy and safety. Therefore, we will systematically compare the efficacy and safety of Danhong in the treatment of cerebral infarction in order to provide reference for clinical application.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 January 2021 and was last updated on 18 January 2021 (registration number INPLASY202110067).

INTRODUCTION

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Condition being studied: Cerebral infarction (CI) is a common and frequent disease with high morbidity and disability rate. Danhong (DH) injection is a standardized product of Traditional Chinese medicine in the treatment of CI. Currently, there is no high-quality evidence to support the efficacy and safety of DH in the treatment of cerebral infarction patients. The purpose of this systematic review protocol is to describe a meta-analysis to evaluate the efficacy of DH in the treatment of CI.

METHODS

Search strategy: Eligible studies in PubMed, MEDLINE, Embase, Cochrane Library Central Register of Controlled Trials, China national knowledge infrastructure database (CNKI), Wan fang database, VIP Database, and SinoMed will be searched by two authors from their inception to July 2020, independently. Moreover, relevant studies in Google scholar and Baidu Scholar will also be retrieved. The search strategy in Pubmed is as follows:1#: Search: (((((((cerebral infarction[Me SH Terms]) OR (stroke[Me SH Terms])) OR (brain ischemia[Me SH Terms])) OR(hypoxia, brain[Me SH Terms])) OR (brain infarction[Me SH Terms])) OR (ischemic cerebral infarction[Title/Abstract])) OR (ischemic stroke[Title/Abstract])) OR (ischemic brain infarction[Title/Abstract]). 2#: Search: (danhong [Me SH Terms]) OR (danhong injection[Title/Abstract]). 3#: Search: (((((((((clinical trials, randomized[MeSH Terms]) OR (randomized controlled trial[MeSH Terms])) OR (controlled clinical trials, randomized[MeSH Terms])) OR (random allocation[MeSH Terms])) OR (RCT[Title/Abstract])) OR (controlled clinical trial[Title/Abstract])) OR (randomized[Title/Abstract]) OR (trial[Title/Abstract]). #1 and #2 and #3.

Participant or population: This study will include patients diagnosed with CI by head computed tomography/ magnetic resonance imaging. Included patients had no restrictions on age, sex, economic status, severity of the disease, or education.

Intervention: Studies in which interventions in-volved DH alone or combined with other routine pharmaco-therapies will be included. In the control group, interventions will include placebo or conventional pharmacotherapies recom-mended by guidelines. Studies with different conventional pharmacotherapies in the control and treatment groups will be excluded.

Comparator: No stretch.

Study designs to be included: In this work, we will include randomized controlled trials (RCTs) of DH of any size and duration in adult populations (>18 years). Non-

randomized control studies and observational study will be excluded. Studies published in English and Chinese will be included.

Eligibility criteria: Study type. In this work, we will include randomized controlled trials (RCTs) of DH of any size and duration in adult populations (>18 years). Non-randomized control studies and observational study will be excluded. Studies published in English and Chinese will be included. Types of patients. This study will include patients diagnosed with CI by head computed tomography/ magnetic resonance imaging. Included patients had no restrictions on age, sex, economic status, severity of the disease, or education. Intervention type. Studies in which interventions in-volved DH alone or combined with other routine pharmaco-therapies will be included. In the control group, interventions will include placebo or conventional pharmacotherapies recom-mended by guidelines. Studies with different conventional pharmacotherapies in the control and treatment groups will be excluded.

Information sources: We will extract and record the first author's name, year of publication, study design, group information, age, gender, dropouts, sample size, duration of intervention, outcomes, and adverse effects from the studies that met the inclusion criteria. We will contact the corresponding authors for additional information if necessary.

Main outcome(s): The criterion of therapeutic efficiency on neurological functions and daily living activities will be assessed by the National Institute of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), activities of daily living (ADL), and Barthel Index (BI). The cognitive functions will be evaluated by mini-mental state examination (MMSE) and Montreal Cognitive Assessment (MoCA).

Quality assessment / Risk of bias analysis: The risk of bias in each included study will be assessed utilizing the Cochrane Collaboration s risk of bias tool. Two researchers will independently evaluate the bias based on the following items: random sequence generation, allocation concealment, blinding of the participants and personnel, blinding of the outcome assessments, incomplete outcome data, selective reporting, and other sources of bias. The studies will be evaluated as low risk, high risk, and unclear risk. Inconsistencies will be resolved by discussion with other reviewers.

Strategy of data synthesis: The Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) will be used to analyze the data. For outcomes, we will use relative risk (RR) and 95% confidence interval (CIs) to evaluate dichotomous outcomes, while using standardized mean difference (SMD) and mean difference (MD) with 95% CIs to assess continuous variables. The heterogeneity between RCTs will be calculated by Cochrane X2 and I2 tests. If P>.05 and I2< 50%, no statistical heterogeneity is observed, the data will be calculated with a fixed-effect model. IfP 50%, the random effect model will be used.

Subgroup analysis: If there is significant heterogeneity, subgroup analysis will be conducted based on different interventions, controls, durations of treatment, and outcome measures.

Sensibility analysis: We will carry out sensitivity analyses to investigate the robustness of the study conclusions. In this way, we will be able to assess the impact of low- quality studies on the overall results and whether the results are robust.

Country(ies) involved: Henan Province, China.

Keywords: cerebral infarction, meta-analysis, protocol, danhong.

Contributions of each author:
Author 1 - Ping Pan.
Author 2 - Yinglin Zhao.
Author 3 - Jinqiu Wang.