INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Efficacy and safety of Naoxintong capsule for acute ischemic stroke: A protocol for systematic review and meta-analysis

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Review question / Objective: **Is Naoxintong capsule efficacy and safety for acute ischemic stroke? P: Patients with acute ischemic stroke; I: Treat with Naoxintong capsule; C: Treat without Naoxintong capsule; O: Curative effects, adverse effects; S: RCT.**
Condition being studied: **Acute ischemic stroke is a common acute cerebrovascular disease which is caused by focal occlusion or stenosis of arteries in the brain, and featured with neurological dysfunction. Due to the high morbidity, mortality and disability rate, acute ischemic stroke has become a global health issue. Although medical thrombolysis and endovascular therapies have been applied in the treatment of acute ischemic stroke, the narrow therapeutic window, risk of bleeding, and ischemia-reperfusion injury limit their application. Naoxintong capsule is a traditional Chinese patent medicine that contains various sixteen traditional Chinese medicines, which is used to treat acute ischemic stroke in China. However, the systematic evaluation on the clinical efficacy and safety of Naoxintong capsule is still absent. Therefore, aiming to assess the quantity, quality and overall strength of existing clinical evidence on Naoxintong capsule in the treatment of acute ischemic stroke, we attempt to perform a systematic review and meta-analysis to identify whether the application of Naoxintong capsule appeared to be adequate reliability regarding on the efficacy and safety.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 August 2021 and was last updated on 13 August 2021 (registration number INPLASY202180052).

INTRODUCTION

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METHODS

Participant or population: Patients with acute ischemic stroke (CT and/or MRI are used to confirm the diagnosis of acute ischemic stroke).

Intervention: Treated with Naoxintong capsule.

Comparator: Treated without Naoxintong Capsule.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: 1. Inclusion criteria: The studies qualified with all inclusion criteria will be consideredfor inclusion. (1) Patients with acute ischemic stroke, regardless of any age and gender; (2) All randomized control trials (RCTs) of Naoxintong capsule for acute ischemic stroke which were published in English and Chinese; (3) Experimental group were treated with Naoxintong capsule, used alone or in combination with other therapies and regardless the dose or duration of administration; (4) Control group can be defined as blank control or placebo control or other intervention control, while Naoxintong capsule treatment was not applied in control group; (5) The outcome measures are National Institutes of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), Barthel Index (BI), mortality, adverse events.2. Exclusion criteria: The studies meet with any of exclusion criteria will be excluded.(1) Cerebral hemorrhage in patients with AIS; (2) Cohort studies, case reports, cross-over, preclinical studies.

Information sources: Both English databases (including Scopus, EMBASE, PubMed, Cochrane library, Google Scholar, and Web of Science) and Chinese databases (including CNKI, VIP, Wanfang, and Chinese Biomedical Literature Database) will be searched for the identification of eligible data. We will search the databases from inception to August 2021. Additionally, potential studies in the reference lists of valid studies will also be considered as the information source for supplement.

Main outcome(s): Neurological impairment (measured as NIHSS and mRS scores).

Additional outcome(s): Dependency (measured as BI score), adverse events, and death.

Quality assessment / Risk of bias analysis: The Cochrane Collaboration Risk of Bias Tool will be used by two independent researchers to evaluate the risk of bias. Disagreement between the two researchers will be arbitrated by a third one.

Strategy of data synthesis: The RevMan 5.3 software will be used for meta-analysis. The relative risk (RR) will be used as the effect index for the dichotomous variable,

standardized mean differences (SMD) will be used as the effect index for the continuous variable. The confidence interval (CI) of each effect index was set to 95%. I2 statistic will be adopted to assess the heterogeneity. If there is heterogeneity between the studies (I2>50%), the random effects model will be selected; Otherwise, the fixed effect model will be utilized. P< 0.05 indicates statistical significance. In addition, if the clinical data provided by the included literatures are incomplete and cannot be systematically evaluated, the descriptive analysis shall be carried out.

Subgroup analysis: When there is obvious heterogeneity in the study, subgroup analysis will be conducted according to the age, gender, treatment course, dosage of included patients, if adequate information could be available from include studies.

Sensitivity analysis: We will use the sensitivity analysis to assess the stability of the findings. Low-quality literature can be excluded for sensitivity analysis.

Country(ies) involved: China.

Keywords: Naoxintong capsule; acute ischemic stroke; meta-analysis; protocol.

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