INPLASY PROTOCOL

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Conflicts of interest: None declared.

INTRODUCTION

Review question / Objective: Some research indicated that the cumulative long-term risk of stroke recurrence was 3.1% at thirty days,11.1% at a year and 26.4% at five year. Moreover, there will be higher risk of death or vascular events for

patients who have ischemic stroke. Also, recently, traditional Chinese medicine has attracted more and more attention for its exact curative effect and low toxicity. In addition, TCM was multi-link, multi-target in pre thrombosis which can prevent the recurrence of ischemic stroke.

Comparison of Traditional Chinese Medicine in the Long-Term Secondary Prevention for Patients with Ischemic Stroke: a Systematic Review and Network Meta-Analysis

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Condition being studied: At present, there are little reviews and meta-analysis on the long-term secondary prevention of ischemic stroke by the combination of traditional Chinese and Western medicine. One of the few studies indicated that Buyang Huanwu decoction has no statistical significance in reducing the recurrence rate of ischemic stroke, possibly because of lack of literature during that time. Additionally, effectiveness in long-term secondary prevention and safety between TCM are also unclear, which cause confusion for physicians.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 May 2021 and was last updated on 10 May 2021 (registration number INPLASY202150036). **Rationale:** According to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

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METHODS

Participant or population: Patients who were diagnosed with ischemic stroke, and there's no limitation on nationality, race, gender, age, disease duration.

Intervention: Traditional Chinese medicine plus conventional western medicine. traditional And Chinese medicine include Naoxintong capsule, Tongxinluo capsule Buyang Huangwu Docation, Naomaitai capsule, Dengzhan Shenmai capsule, Naoshuantong capsule, Maixuekang capsule.

Comparator: Another kind of traditional Chinese medicine plus conventional western medicine or conventional western medicine alone. Also, the common conventional western drugs were Antiplatelet drugs, Statins Antihypertensive drugs, Hypoglycemic drugs and so on.

Study designs to be included: Only RCTs.

Eligibility criteria: (1) Participants: patients who were diagnosed with ischemic stroke, and there's no limitation on nationality, race, gender, age, disease duration; (2) Interventions and comparisons: the treatment group was given traditional Chinese medicine plus conventional western medicine, and the control group adopted another kind of traditional Chinese medicine plus conventional western medicine or conventional western medicine alone. Also, the conventional western medicine treatment must be consistent between treatment and control group. Besides, the common conventional western medicine drugs were Statins Antihypertensive drugs, Antiplatelet drugs, Hypoglycemic drugs and so on. And traditional Chinese medicine include Naoxintong capsule. Tongxinluo capsule Buyang Huangwu Docation, Naomaitai capsule, Dengzhan Shenmai capsule, Naoshuantong capsule, Maixuekang capsule. Furthermore, there's no limitations on dosage and Medication time; (3) Outcomes: the primary outcomes of this network meta-analysis were recurrent stroke and National Institute of Health stroke scale, and the secondary outcomes were fibrinogen, fasting plasma glucose, triglycerides, cholesterol. Moreover, the safety outcomes were all-cause mortality and Adverse events. In this network metaanalysis, RCT which included one of the primary outcomes was sufficient. (4) Study design: only RCTs were taken into our consideration.

Information sources: PubMed, Web of Science, Embase, the China National Knowledge Infrastructure (CNKI), the Chinese Biological Medicine Literature Service System (CBM), the Chinese Scientific Journal Full-text Database (VIP), and the Wan-fang Database (WF).

Main outcome(s): Recurrent stroke, NIHSS.

Additional outcome(s): Fibrinogen, fasting plasma glucose, triglycerides, cholesterol, all-cause mortality and adverse events.

Data management: Endnote 20 was used to manage retrived literatures stata 16.0 was used to perform network meta-analysis and make graphs.

Quality assessment / Risk of bias analysis: Cochrane risk of bias tool and GRADE assessment. **Strategy of data synthesis:** It followed the Preferred Reporting Items for Systematic Review and Meta- Analysis (PRISMA).

Subgroup analysis: Subgroup analysis was did for primary outcomes First: age=60 Second: low dose medicine, medium dose medicine, high dose medicine.

Sensitivity analysis: sensitivity analysis was did for primary outcomes First: age=60 Second: low dose medicine, medium dose medicine, high dose medicine.

Language: No language limitation.

Country(ies) involved: China.

Keywords: network meta-analysis, traditional Chinese medicine, ischemic stroke, secondary prevention, stroke risk factors.

Contributions of each author:

Author 1 - Jiali Li. Author 2 - Li Yu. Author 3 - Weifeng Jin. Author 4 - Xiaohong Li.