INPLASY PROTOCOL

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Corresponding author:
Qingshan Liu

nlqsh@163.com

Author Affiliation:
Minzu University of China.

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None declared.

The Efficacy and Safety of Employed Treatments for Ischemic Stroke: An Umbrella Review

Li, YB[1]; Cui, RY[2]; Fan, FC[3]; Lu, YY[4]; Ai, YW[5]; Liu, H[6]; Liu, SB[7]; Du, Y[8]; Qing, ZP[9]; Sun, WJ[10]; Yu, QQ[11]; Liu, QS[12]; Cheng, Y[13].

Review question / Objective: **Ischemic stroke is a leading cause of morbidity and mortality. There are constantly emerging new studies of employed treatments for ischemic stroke, and some results are conflicting. Therefore, it is necessary to summarize and analyze the latest published clinical research data. The present study aimed to perform an umbrella review of the systematic reviews and meta-analyses of stroke therapies through a comprehensive and updated literature search, and to reach a definitive conclusion by integrating all available meta-analyses to identify which of the commercially available treatments for ischemic stroke patients are efficacious and safe.**
Eligibility criteria: **We included meta-analyses and systematic reviews that determined the efficacy and safety of treatments in patients with stroke. Inclusion criteria were: 1) written in English; 2) published systematic review or meta-analyses; 3) including any evaluation of clinical assessment scales for stroke; 4) published in peer-reviewed journals. Studies were excluded if 1) unpublished studies; 2) no necessary sample data; 3)patients were diagnosed with other stroke; 4) study reported insufficient details and other outcomes; 5) study presence risk of bias/study limitations.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 May 2022 and was last updated on 26 May 2022 (registration number INPLASY202250145).

INTRODUCTION

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present study aimed to perform an umbrella review of the systematic reviews and meta-analyses of stroke therapies through a comprehensive and updated literature search, and to reach a definitive conclusion by integrating all available meta-analyses to identify which of the commercially available treatments for ischemic stroke patients are efficacious and safe.

Condition being studied: Ischemic stroke is a major cause of death and disability, so prevention and effective treatment of stroke are of utmost importance in China and in the west. Approximately one-third of strokes are fatal, and another third leave survivors with permanent disability. However, little is known about the efficacy and safety of employed treatments of ischemic stroke in the hyper-acute (0-24 h) and acute phases (1-7 days) and recovery period (>7 days) post-stroke in humans. The World Health Organization has suggested that an incidence of stroke occurs once every five seconds worldwide. Moreover, around 15 million cases of stroke occur each year, and with one-third of affected individuals losing their life (equivalent to approximately 11% of all deaths) and another one-third becoming permanently disabled, this places a significant burden on families and communities. The key challenge in the treatment of stroke is to identify the most effective way to implement the efficacious interventions currently available.

METHODS

Participant or population: Ischemicstroke.

Intervention: Efficacy and Safety of Employed Treatments for Ischemic Stroke.

Comparator: We examined global neurological deficit, neurological function deficit and cognitive function scores, quality of life, and activities of daily living as efficacy endpoints, and the incidence of adverse events as safety profiles.

Study designs to be included: We conducted a search for meta-analyses and systematic reviews on PubMed, the Cochrane Library, and Web of Science to address this knowledge gap. We examined global neurological deficit, neurological function deficit and cognitive function scores, quality of life, and activities of daily living as efficacy endpoints, and the incidence of adverse events as safety profiles.

Eligibility criteria: We included meta-analyses and systematic reviews that determined the efficacy and safety of treatments in patients with stroke. Inclusion criteria were: 1) written in English; 2) published systematic review or meta-analyses; 3) including any evaluation of clinical assessment scales for stroke; 4) published in peer-reviewed journals. Studies were excluded if 1) unpublished studies; 2) no necessary sample data; 3)patients were diagnosed with other stroke; 4) study reported insufficient details and other outcomes; 5) study presence risk of bias/study limitations.

Information sources: A systematic search of published peer-reviewed English-language literature was conducted using PubMed, Web of Science, and the Cochrane Library until March 2022. The database search terms were as follows: (Ischemic stroke) and (systematic review or meta-analysis) and clinical trial. We included meta-analyses and systematic reviews that determined the efficacy and safety of treatments in patients with stroke. The AMSTAR2 tool was used to evaluate systematic reviews and meta-analyses. The methodological quality of the studies was determined by the percentage of AMSTAR2 score. The percentage of AMSTAR2 score was classified into 0–33%, 34–66%, and 67%–100% indicating low quality, medium quality, and high quality, respectively. We searched for related articles using keywords and filtering titles, and two investigators screened the literature independently. Articles were downloaded and the abstracts screened using inclusion criteria, deleting any irrelevant or repetitive articles. Thereafter, we manually searched the reference lists of the chosen papers for any other relevant studies not found in our

initial search. Finally, a full-text search was performed to extract and then analyse the data from articles.

Main outcome(s): Sixteen eligible papers, including 374 studies, were included in the umbrella review. The results showed that thrombolytic therapy (human urinary kallidinogenase, alteplase, tenecteplase, desmoteplase), antiplatelet agents (aspirin, clopidogrel, tirofiban), statins, heparin, MSCs, edaravone and blood-activating and stasis-dispelling herbs (NaoShuanTong capsule, Ginkgo biloba, Dengzhan Shengmai, Xuesaitong injection, Muoluoning) demonstrated undeniable positive effects in clinical effective rate, and in NIHSS, mRS, BI and neurological deficit scores. Furthermore, ischemic stroke agents were found likely to have an important effect on increasing neurological function or activities of daily living in mild to moderate ischemic stroke patients.

Quality assessment / Risk of bias analysis: Three investigators (Yongbiao Li, Ruyi Cui, Fangcheng Fan.) independently selected those trials that met the inclusion criteria and extracted details of dosage, intention to treat analysis, number lost to follow-up, treatment duration, methods, interventions, outcomes, study presence risk of bias/ study limitations and results. Data were obtained from the authors whenever possible.

Strategy of data synthesis: The sample size and mean difference were used to calculate the four clinical assessment scales. NIHSS/ mRS/BI/NFD scores were used to evaluate of neurological status, behavioral symptoms in patients were calculated by NFDS. We focused on the clinical effect is divided into essentially recovered, significant improvement, no change, deterioration; cognitive function scoring; quality of life as activities of daily living. The adverse events were assessed incidence of adverse events, and the OR were calculated. Therefore, mean difference or odds ratio with 95% CI and p values were used to assess the efficacy and safety of the study medications.

Subgroup analysis: We searched for related articles using keywords and filtering titles, and two investigators screened the literature independently. Articles were downloaded and the abstracts screened using inclusion criteria, deleting any irrelevant or repetitive articles. Thereafter, we manually searched the reference lists of the chosen papers for any other relevant studies not found in our initial search. Finally, a full-text search was performed to extract and then analyse the data from articles.

Sensitivity analysis: The AMSTAR2 tool was used to evaluate systematic reviews and meta-analyses{De Santis, 2021 #58}. The methodological quality of the studies was determined by the percentage of AMSTAR2 score. The percentage of AMSTAR2 score was classified into 0–33%, 34–66%, and 67%–100% indicating low quality, medium quality, and high quality, respectively.

Language: Written in English.

Country(ies) involved: China.

Keywords: ischemic stroke, clinical trial, systematic review, umbrella review, neurological functional.

Contributions of each author:
Author 1 - Yongbiao li.
Author 2 - Ruyi Cui.
Author 3 - Fangcheng Fan.
Author 4 - Yangyang Lu.
Author 5 - Yangwen Ai.
Author 6 - Hua Liu.
Author 7 - Shaobo Liu.
Author 8 - Yang Du.
Author 9 - Zhiping Qin.
Author 10 - Wenjing Sun.
Author 11 - Qianqian Yu.
Author 12 - Qingshan Liu.
Author 13 - Yong Cheng.