INPLASY PROTOCOL

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Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None.

Effect of hirudin on serum matrix metalloproteinase-9 of acute cerebral infarction: a protocol of systematic review and meta-analysis

Bian, Y[1]; Zhang, Y[2]; Tian, ZB[3].

Review question / Objective: **Does hirudin have effect on serum matrix metalloproteinase-9 (SMMP9) of acute cerebral infarction (ACI)?**
Condition being studied: **Hirudin; serum matrix metalloproteinase-9; acute cerebral infarction.**
Information sources: **We will perform electronic search form the following electronic databases: from their inceptions to the March 31, 2020: MEDLINE, EMBASE, Cochrane Library, CINAHL, WANGFANG database, VIP database, CBM database, and China National Knowledge Infrastructure. No limitations will be imposed on the language and publication status. The sample of search strategy of MEDLINE is built. Similar search strategies of other electronic databases will be adapted and modified in this study. In addition, we will also search conference proceedings, clinical trial registries, and reference lists of included studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 April 2020 and was last updated on 22 April 2020 (registration number INPLASY202040143).

INTRODUCTION

Review question / Objective: **Does hirudin have effect on serum matrix metalloproteinase-9 (SMMP9) of acute cerebral infarction (ACI)?**

Condition being studied: **Hirudin; serum matrix metalloproteinase-9; acute cerebral infarction.**

METHODS

Participant or population: We will include case-controlled studies (CCSs) on participants that are diagnosed as ACI. The race, gender, age, severity and duration of CCSs are not restricted.

Intervention: We will include studies using hirudin in patients with ACI in the experimental group.

Comparator: We will consider studies using any management in patients with ACI in the control group.

Study designs to be included: Only CCSs will be included in his study. Other studies, such as animal studies, case studies, reviews, and non-CCSs will be excluded.

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Main outcome(s): The primary outcome is SMMP9, as measured by enzyme linked immunoassay kit or other methods. The secondary outcomes are plasma positive pentamer protein 3, tissue plasminogen activator, high-sensitivity C-reactive protein level, hemorheology index, thromboplastin time, plasma prothrombin time, plasminogen activator inhibitor, thromboxane B2, improvement in neurological deficits (as checked by Simple Intelligence Status Check Scale, or other scales), and quality of life (as assessed by Activities of Daily Living).

Data management: Two investigators will independently carry out data extraction, respectively. Any disagreements regarding the data extraction between two investigators will be resolved by another investigator. We will extract the following information: basic characteristics, including first author, time of publication, region, age and sex of patients, diagnostic criteria, inclusion and exclusion criteria, et al; study methods; details of managements, including types of interventions and controls, dosage, frequency, et al; all primary and secondary outcomes, and any other relevant information. If we identify some unclear or missing data, primary corresponding authors will be contacted to require these data.

Quality assessment / Risk of bias analysis: The methodological quality of all included studies will be assessed by two independent investigators using Cochrane Risk of Bias Tool. It consists of 7 domains, and the judgments on each item is categorized as low risk of bias, unclear risk of bias, and high risk of bias. Any disagreements between two investigators will be solved by negotiation or consultation with the help of another investigator.

Strategy of data synthesis: RevMan 5.3 software is used for statistical analysis. Mean difference or standardized mean difference and 95% confidence intervals (CIs) will be used for expressing quantitative data, and risk ratio and 95% CIs will be utilized for exerting dichotomous data. We will apply I^2 statistic test to check statistical heterogeneity across studies. If $I^2 \leq 50$, which means reasonable heterogeneity, while if $I^2 > 50\%$, which suggests substantial heterogeneity. When $I^2 \leq 50$, we will use a fixed-effects model. Otherwise, a random-effects model will be utilized. If sufficient data are obtained from at least two included studies, we will pool the data and will

perform meta-analysis if reasonable heterogeneity is identified. If not, we will undertake subgroup analysis to check the factors for such substantial heterogeneity.

Subgroup analysis: We will explore the subgroup analysis according to on the different basic characteristics, study qualities, interventions, controls and outcome measurements.

Sensibility analysis: We will undertake sensitivity analysis to check robustness of merged results by removing low quality studies.

Country(ies) involved: China.

Keywords: Hirudin; serum matrix metalloproteinase-9; acute cerebral infarction; effect.