INPLASY PROTOCOL

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Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None.

Efficacy of statins in the prevention of epilepsy: a systematic review and meta-analysis of cohort studies

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Review question / Objective: **A systematic review and meta-analysis of prevention in acquired epilepsy after brain insults.**
Condition being studied: **Epilepsy, a common neurological disorders, affacting approximately 50 million people worldwide, is a major impact on society and global health. Previous clinical trial have found that prophylactic use of an anti-epileptic drug for prolonged periods unable to prevent the development of epilepsy after brain insults. Hydroxymethyl - glutaryl–coenzyme A reductase inhibitors (statins) are one of the most pre-scribed classes of cardiovascular medications. Interestingly, statins have also been shown to beprotective in neurologic disorders. Thus, we aim to assess the potential efficacy of statins in the prevention of acquired epilepsy after brain insults.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 September 2020 and was last updated on 23 September 2020 (registration number INPLASY202090085).

INTRODUCTION

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statins have also been shown to beprotective in neurologic disorders. Thus, we aim to assess the potential efficacy of statins in the prevention of acquired epilepsy after brain insults.

METHODS

Search strategy: The search string will be built as follows: #1 Search: "Hydroxymethylglutaryl-CoA Reductase Inhibitors"[Mesh] #2 Search: Hydroxymethylglutaryl-CoA Reductase Inhibitor* OR hmg-coa reductase inhibitor* OR Hydroxymethylglutaryl Coenzyme a Reductase Inhibitor*[tiab] #3 Search: statin OR statins OR simvastatin OR atorvastatin OR pravastatin OR fluvastatin OR cerivastatin OR rosuvastatin OR lovastatin OR fluindostatin OR mevastatin OR pitavastatin OR compactin OR dalvastatin OR mevinolin OR meglutol[tiab] #4 Search: #1 OR #2 OR #3 #5 Search: "Epilepsy"[Mesh] #6 Search: "Seizures"[Mesh] #7 Search: epilep* OR seizure* OR convuls*[tiab] #8 Search: #5 OR #6 OR #7 #9 Search: #4 AND #8.

Participant or population: Patients with newly-onset brain insults and no history of epilepsy before were enrolled.

Intervention: Statin treatment was the main intervention (e.g. Anytime, Pre-brain insults and Acutely only).

Comparator: Blank control.

Study designs to be included: Randomized controlled trials and cohort studies will be included.

Eligibility criteria: We included full-text articles or conference proceedings that met the following criteria: reported the efficacy (using outcomes such as seizure freedom or frequency) of statins in the prevention of acquired epilepsy after brain insults in adult patients (age over 18) or tolerability (using outcomes such as number of side effects or proportion of patients discontinuing medication due to side effects) of stains. Studies were excluded if the acquired epilepsy was not reported and could not be calculated from the data provided or if the study did not distinguish between early and late seizures.

Information sources: We will search, with no time restrictions, the following databases for relevant English language literature: PubMed, EMBASE, the Cochrane Central Register of Controlled Trials.

Main outcome(s): The incidence of seizures and epilepsy.

Quality assessment / Risk of bias analysis: The methodological quality of RCT was assessed using the Cochrane risk of bias tool, and the Newcastle–Ottawa quality assessment scale (NOS) was adopted for cohort studies.

Strategy of data synthesis: We extracted unadjusted estimates of the rate of seizures and epilepsy, used random effects analyses to calculate the pooled estimate and 95% confidence interval, and to assessed heterogeneity with the I2 statistic.

Subgroup analysis: We conducted subgroup analyses to assess differences in the following subgroups: statins use of time-dependent variable (anytime, pre-brain insults, acutely only), lipophilic statins vs hydrophilic statins, and the intensity of statin therapy (low, moderate to high).

Sensibility analysis: If p value < 0.1 in the chi-square test or I2 was greater than 30%, which was considered to be high heterogeneity, sensitivity analysis should be conducted. To observe the comprehensive effect whether significantly change after the inclusion of the study was eliminated one by one.

Country(ies) involved: China.

Keywords: Statin; Epilepsy; Seizures; Stroke; Meta-analysis.

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