INPLASY PROTOCOL

To cite: Liu et al. Cilostazol for Aneurysmal Subarachnoid Hemorrhage: an Update Systematic Review and Meta-analysis. Inplasy protocol 2020100110. doi: 10.37766/inplasy2020.10.0110

Received: 27 October 2020

Published: 28 October 2020

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Support: **No.**

Review Stage at time of this submission: **Data analysis.**

Conflicts of interest: **No.**

Cilostazol for Aneurysmal Subarachnoid Hemorrhage: an Update Systematic Review and Meta-analysis

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Review question / Objective: **To evaluate whether cilostazol improves the outcomes of patients with aneurysmal subarachnoid hemorrhage(aSAH): P: The patients with aSAH caused by a ruptured aneurysm. I: Patients in the experimental group will be treated with cilostazol. C: Comparisons were to aSAH patients without cilostazol. O: The primary outcome was clinical favourable outcomes, the secondary outcomes included severe angiographic vasospasm, symptomatic vasospasm, new cerebral infarction and mortality. Furthermore, we examined whether clinical outcomes were associated with the dosage of cilostazol (300mg/day vs 100-200mg/day) S:Randomized control study and observational study were included.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 October 2020 and was last updated on 28 October 2020 (registration number INPLASY2020100110).

INTRODUCTION

Review question / Objective: **To evaluate whether cilostazol improves the outcomes of patients with aneurysmal subarachnoid hemorrhage(aSAH): P: The patients with aSAH caused by a ruptured aneurysm. I: Patients in the experimental group will be treated with cilostazol. C: Comparisons were to aSAH patients without cilostazol. O: The primary outcome was clinical favourable outcomes, the secondary outcomes included severe angiographic vasospasm, symptomatic vasospasm, new**

cerebral infarction and mortality. Furthermore, we examined whether clinical outcomes were associated with the dosage of cilostazol (300mg/day vs 100-200mg/day) S:Randomized control study and observational study were included.

Condition being studied: Aneurysmal subarachnoid hemorrhage (aSAH) is a serious condition that affects not just the brain, but multiple other organ systems as well . Despite a steady reduction of mortality from acute SAH in recent years, this entity is still associated with considerable morbidity and mortality.Delayed cerebral ischemia (DCI) is the main cause of death and disability in patients with aSAH. At present, nimodipine is the most commonly used for the treatment of DCI in most countries. Nimodipine can reduce the incidence of cerebral infarction and improve the prognosis of patients with aSAH, but it cannot reduce the occurrence of vasospasm. Application of cilostazol was reported to ameliorate vasospasm and improve outcomes in series and clinical trials.Prior systematic reviews examining this treatment have had limitations.

METHODS

Search strategy: We searched PubMed, Embase, Medline and the Cochrane Library through August 2020.Terms we used included :"Subarachnoid Hemorrhage","aneurysm","SAH","cilostazol", combined with Boolean operators as appropriate.We restricted our analysis to articles written in English.

Participant or population: A adult patients (aged 18 years or older) with the diagnosis of aSAH.

Intervention: Patients in the experimental group will be treated with cilostazol.

Comparator: Comparisons were to aSAH patients without cilostazol. The other treatment measures were the same as the experimental group.

Study designs to be included: Randomized control study and observational study.

Eligibility criteria: Inclusion criteria: (1) researched on adult patients (aged 18 years or older) with the diagnosis of aSAH; (2) applied cilostazol in the treatment group as the main therapy; (3) compared with the control group without cilostazol; (4) described the number of patients and events of interest in each group.

Information sources: Searching through PubMed, Embase, Medlline and Cochrane library database.

Main outcome(s): The primary outcome was clinical favourable outcomes.

Additional outcome(s): The secondary outcomes included severe angiographic vasospasm, symptomatic vasospasm, new cerebral infarction and mortality. Furthermore, we examined whether clinical outcomes were associated with the dosage of cilostazol (300mg/day vs 100-200mg/day).

Quality assessment / Risk of bias analysis: The randomized control study and observational study were assessed by the Cochrane collaboration's tool and Newcastle Ottawa scale, respectively.

Strategy of data synthesis: Two investigators (Liu J.F. and He J.L.) independently extracted the following information from each eligible article: name of the first author, study design, study location(country),study period, follow-up time, treatment modalities and baseline characteristics of patients (eg, mean age of participants, number of participants, surgery type, severity assessment of participants).Disagreements between the 2 investigators were resolved by consultation with senior author(Hou D.R.).

Subgroup analysis: Subgroup analysis will be performed in different types of studies and Clinical outcomes of different doses of cilostazol.

Sensibility analysis: I2 values exceeding 25%,50% and 75% represent low, moderate and high heterogeneity, respectively. Sensitivity analyses were conducted by sequentially excluding one study at a time to check whether the results were robust.

Language: English.

Country(ies) involved: Japan.

Other relevant information: cilostazol, aneurysm, subarachnoid hemorrhage, meta-analysis.

Keywords: cilostazol, aneurysm, subarachnoid hemorrhage, meta-analysis.

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