INPLASY PROTOCOL

To cite: Ren et al. Effect of Sodium-glucose cotransport-2 inhibitors on lowering blood pressure in patients with hypertension and pre-hypertension: A meta-analysis. Inplasy protocol 202120004. doi: 10.37766/inplasy2021.2.0004

Received: 01 February 2021

Published: 01 February 2021

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Support: **None.**

Review Stage at time of this submission: **Piloting of the study selection process.**

Conflicts of interest:
None declared.

Effect of Sodium-glucose cotransport-2 inhibitors on lowering blood pressure in patients with hypertension and pre-hypertension: A meta-analysis

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Review question / Objective: **The aim of this meta-analysis of randomized controlled trials is to evaluate the efficacy of SGLT2 inhibitors on lowering blood pressure in patients with hypertension and pre-hypertension.**
Condition being studied: **Recently, a new class of drugs, the sodium glucose co-transporter (SGLT)-2 inhibitors, has been used to treat patients with type 2 diabetes. Some trials show that SGLT-2 inhibitors may confer cardiovascular protection, including a reduction in blood pressure (BP). Pre-hypertension and early hypertension is a crucial stage in the prevention and treatment of hypertension. Pharmacotherapy for pre-hypertension and early hypertension has been paid more and more attention.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 February 2021 and was last updated on 16 February 2021 (registration number INPLASY202120004).

INTRODUCTION

Review question / Objective: **The aim of this meta-analysis of randomized controlled trials is to evaluate the efficacy of SGLT2 inhibitors on lowering blood pressure in patients with hypertension and pre-hypertension.**

Condition being studied: **Recently, a new class of drugs, the sodium glucose co-transporter (SGLT)-2 inhibitors, has been used to treat patients with type 2 diabetes. Some trials show that SGLT-2 inhibitors may confer cardiovascular protection, including a reduction in blood pressure (BP). Pre-hypertension and early**

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METHODS

Search strategy: We will search, with no time restrictions, the following databases for relevant English language literature: PubMed (MEDLINE), the Cochrane Central Register of Controlled Trials (CENTRAL) and Embase. The search string will be built as follows: (SGLT2 inhibitors OR Gliflozins) AND (Hypertension OR Blood Pressure OR Pre-hypertension). The electronic database search will be supplemented by a manual search of the reference lists of included articles.

Participant or population: Adults with hypertension or pre-hypertension (resting systolic BP≥120 mmHg and/or diastolic BP ≥ 80 mmHg or administrating a stable regimen of an anti-hypertension for ≥4weeks before screening) will be included.

Intervention: Using of SGLT2 inhibitors was the main intervention.

Comparator: Placebo or blank controller was the comparator.

Study designs to be included: Randomized controlled trials will be included.

Eligibility criteria: 1. Subjects were adults with resting systolic BP≥120 mmHg and/or diastolic BP≥80 mmHg or administrating a stable regimen of an anti-hypertension for ≥4weeks before screening. 2. The intervention group was treated with SGLT2 inhibitors. 3. Control group was included, including placebo or blank control group 4. Change in office blood pressure was assessed. 5. The study type was RCT.

Information sources: The following databases will be included: PubMed (MEDLINE), the Cochrane Central Register of Controlled Trials (CENTRAL) and Embase.

Main outcome(s): Mean change in resting blood pressure.

Quality assessment / Risk of bias analysis: Two reviewers will independently assess the quality of the selected studies according to the Cochrane Collaboration's tool for randomized controlled trials. Items will be evaluated in three categories: Low risk of bias, unclear bias and high risk of bias. The following characteristics will be evaluated: Random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other biases. Results from these questions will be graphed and assessed using Review Manager 5.4.

Strategy of data synthesis: Risk ratio (RR) for both fixed and random effects models (weighting by inverse of variance) will be used. A continuity correction will also be used for cells with zero values. Between-study heterogeneity will be assessed using the $\chi 2$ (Cochran Q) and I2 statistics. According to the Cochrane handbook, the I2 will be considered non-important (60%). Results will be assessed using forest plots and presented as mean differences (MD) for the main outcome and secondary outcomes. An influence analysis will be performed to ascertain the results of the meta-analysis by excluding each of the individual studies. Statistical analysis will be conducted using Review Manager 5.4.

Subgroup analysis: We will consider subgroups such as types of SGLT2 inhibitors, blood pressure levels and location.

Sensitivity analysis: The included studies will be deleted one by one. Then, new meta-analyses were performed to compare the effect size and heterogeneity. If the heterogeneity changes after the deletion of a study, and the effect size is still statistically significant, the study is considered to have heterogeneity. And then, further comparative analysis of the source of heterogeneity is required. If the

effect value and heterogeneity changes were not obvious after each study was deleted one by one, it could indicate that the study results were stable and reliable.

Language: English.

Country(ies) involved: China.

Keywords: Sodium-glucose cotransport-2 inhibitors; blood pressure; meta-analysis.

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