INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Efficacy and safety of Huangkui capsule for diabetic nephropathy A protocol for systematic review and meta-analysis

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Review question / Objective: **This study aims to perform meta-analysis to systematically review the efficacy and safety of Huangkui capsule for diabetic nephropathy.**
Condition being studied: **Diabetic nephropathy is one of the most serious complications of diabetes mellitus and the leading cause of end-stage renal disease in the world. Huangkui capsule, extracted from Abelmoschus manihot (L.) medic (AM), has been widely used to treat DN. However, there is no consensus on the efficacy of Huangkui capsule for DN.**
Information sources: **A comprehensive search of electronic databases is carried out from the initiation of the databases to May 2021. Following total 9 English and Chinese databases will be searched: PubMed, web of science, MEDLINE, Embase, Cochrane Library, China National Knowledge Infrastructure, Chinese Scientific Journals Database (VIP), Wanfang data and Chinese BioMedicine Literature Database.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 June 2021 and was last updated on 17 June 2021 (registration number INPLASY202160057).

INTRODUCTION

Review question / Objective: **This study aims to perform meta-analysis to systematically review the efficacy and safety of Huangkui capsule for diabetic nephropathy.**

Condition being studied: **Diabetic nephropathy is one of the most serious complications of diabetes mellitus and the leading cause of end-stage renal disease in the world. Huangkui capsule, extracted from Abelmoschus manihot (L.) medic (AM), has been widely used to treat DN.**

However, there is no consensus on the efficacy of Huangkui capsule for DN.

METHODS

Search strategy: A comprehensive search of electronic databases is carried out from the initiation of the databases to May 2021. Following total 9 English and Chinese databases will be searched: PubMed, web of science, MEDLINE, Embase, Cochrane Library, China National Knowledge Infrastructure, Chinese Scientific Journals Database (VIP), Wanfang data and Chinese BioMedicine Literature Database. Based on the principle of combination of heading terms and free words, two reviewers will manually search of the following terms using Boolean logic (AND, OR, or NOT):" Huangkui capsule", "Huangkui", "abelmoschus manihot", "Diabetic nephropathy", "Diabetic Kidney Disease", "DN", "RCT", "randomized controlled trial". Disagreements will be resolved through a discussion with a third reviewer. Table 1 presents the retrieval strategy in PubMed. We will retrieve additional relevant publications by searching reference list.

Participant or population: All patients with a clinically diagnosis of DN were included regardless of course of disease, gender, age, race, nationality, education, or economic status.

Intervention: The interventions of control group were as follows: conventional drugs (such as hypoglycemic, antihypertensive), placebo or only diet and exercise control treatment. The experimental group was added with Huangkui capsule based on the control group. There is no restriction of drug dosage, time, frequency or duration of treatment in this study.

Comparator: The primary outcome is efficacy indicators including the total clinical effective rate, 24-h urinary total protein, serum creatinine, blood urea nitrogen, urine albumin excretion rate. The secondary outcome is safety indicators, including adverse reaction rate.

Study designs to be included: All randomized controlled trials (RCTs) of Huangkui Capsule alone or combined with other drugs for DN regardless of blinding, allocation concealment will be included. Studies will not be restricted by publication time and area. The language is limited to Chinese and English.

Eligibility criteria: Types of studies. All randomized controlled trials (RCTs) of Huangkui Capsule alone or combined with other drugs for DN regardless of blinding, allocation concealment will be included. Studies will not be restricted by publication time and area. The language is limited to Chinese and English. 2.2.2. Types of participants. All patients with a clinically diagnosis of DN were included regardless of course of disease, gender, age, race, nationality, education, or economic status. 2.2.3. Types of interventions. The interventions of control group were as follows: conventional drugs (such as hypoglycemic, antihypertensive), placebo or only diet and exercise control treatment. The experimental group was added with Huangkui capsule based on the control group. There is no restriction of drug dosage, time, frequency or duration of treatment in this study. 2.2.4. Types of outcome measures. The primary outcome is efficacy indicators including the total clinical effective rate (calculated by the recovery of biochemical indicators and clinical symptoms), 24-h urinary total protein, serum creatinine, blood urea nitrogen, urine albumin excretion rate. The secondary outcome is safety indicators, including adverse reaction rate.

Information sources: A comprehensive search of electronic databases is carried out from the initiation of the databases to May 2021. Following total 9 English and Chinese databases will be searched: PubMed, web of science, MEDLINE, Embase, Cochrane Library, China National Knowledge Infrastructure, Chinese Scientific Journals Database (VIP), Wanfang data and Chinese BioMedicine Literature Database.

Main outcome(s): The main outcome is efficacy indicators including the total clinical effective rate (calculated by the recovery of biochemical indicators and clinical symptoms), 24-h urinary total protein, serum creatinine, blood urea nitrogen, urine albumin excretion rate.

Additional outcome(s): The secondary outcome is safety indicators, including adverse reaction rate.

Data management: Based on the principle of combination of heading terms and free words, two reviewers will manually search of the following terms using Boolean logic (AND, OR, or NOT):" Huangkui capsule", "Huangkui", "abelmoschus manihot", "Diabetic nephropathy", "Diabetic Kidney Disease", "DN", "RCT", "randomized controlled trial". Disagreements will be resolved through a discussion with a third reviewer.

Quality assessment / Risk of bias analysis: Cochrane Collaboration's tool 5.1.0. will be used to examine the risk of bias. Two reviewers separately conduct the evaluation from the following 7 domains: (1) Randomized sequence generation; (2) Allocation sequence concealment; (3) Blinding of participants and personnel; (4) Blinding of outcome assessment; (5) Incomplete outcome data; (6) Selective outcome reporting; (7) Other biases. A bias value of "L (low risk)", "U (unclear risk)" or "H (high risk)" will be adopted to rank the risk of bias. In the absence of consensus, the final decision is made by the third reviewer.

Strategy of data synthesis: The meta-analysis will be performed with Review Manager Version 5.4 software. The mean difference (MD) or standardized mean differences will be to adopted measure the effect for continuous variables. Risk ratios (RR) or odds ratio (OR)will be assumed to calculate the curative effect for dichotomous variables, with both having 95% confidence intervals (95% CI). I2 test is be used to determine the heterogeneity. The study was considered to be homogeneous when I2≤50%, P≥.1, a fixed effect model is selected for meta-analysis. Otherwise, If I2>50%, P<.1, there was significant statistical heterogeneity in the study and the random-effect model will be used.

Subgroup analysis: Subgroup analysis will be performed if data are available and sufficient, such as different intervention time, different stages of diabetic nephropathy and different outcomes.

Sensitivity analysis: We will undertake a sensitivity analysis to judge the robustness and stability of the review results. The method is that deleting low quality study one by one based on sample size, the risk of bias, missing data and methodological quality.

Country(ies) involved: China.

Keywords: Huangkui capsule, diabetic nephropathy, protocol, meta-analysis, systematic review, efficacy and safety.

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