INPLASY PROTOCOL

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None declared.

Keluoxin capsule for diabetic kidney disease: A protocol for systematic review and meta-analysis

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Review question / Objective: **1. Participants - Adult participants definitely diagnosed with DKD will be included. 2. Interventions - Treatment with keluoxin capsule is the main intervention. 3. Control - The control consists of any western medicine, placebo, or no intervention. 4. Outcome - The main outcome will be the mean change in albuminuria and eGFR. 5. Study design - A systematic review and meta-analysis will be conducted.**
Information sources: **PubMed, Cochrane Library, EMBASE, China National Knowledge Infrastructure, WANFANG database, VIP, SinoMED, and Chinese Biomedical Literature Database (CBM) will be searched to ensure all possible RCT studies on keluoxin capsule, without limitation of the language.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 November 2021 and was last updated on 17 November 2021 (registration number INPLASY2021110067).

INTRODUCTION

Review question / Objective: **1. Participants - Adult participants definitely diagnosed with DKD will be included. 2. Interventions - Treatment with keluoxin capsule is the main intervention. 3. Control - The control consists of any western medicine, placebo, or no intervention. 4. Outcome - The main outcome will be the mean change in albuminuria and eGFR. 5. Study design - A systematic review and meta-analysis will be conducted.**

Condition being studied: **Diabetic kidney disease (DKD), which is a serious complication of DM defined as persistent albuminuria or reduced estimated using different formulas (eGFR), affects 30-40% individuals with diabetes and approximately 50% of them can progress to end-stage renal disease (ESRD).**

Improving albuminuria and reduced eGFR in DKD patients has become an important treatment to delay the progress to ESRD. Several cross-sectional studies have shown an increasing use of glucose-lowering medications, RAS blockers, and statins, resulting in a progressive improvement in glycemic, blood pressure and lipid control, leads to the reduction in the prevalence of albuminuria and the increment in the prevalence of reduced eGFR. However, these therapies for DKD also lead to an increased risk of significant side effects such as hyperkalemia associated with RAS blockade , genital mycotic infections, hypoglycemia, and diabetic ketoacidosis caused by SGLT2 inhibitors, suggesting that additive effects may also cause harm. Chinese medicine has been shown a great beneficial effect on reduction of albuminuria and renal function, and safe in the treatment of DKD. Keluoxin capsule, a Chinese patent medicine used for DKD, could improve proteinuria and protect renal function in the DKD patients without obvious side effect. At present, there are several clinical trails of Keluoxin capsule, but its efficacy and safety for DKD have not been objectively evaluated.

METHODS

Participant or population: Adult participants definitely diagnosed with DKD will be included.

Intervention: Treatment with keluoxin capsule is the main intervention.

Comparator: The control consists of any western medicine, placebo, or no intervention.

Study designs to be included: Randomized controlled trials (RCTs) will be included.

Eligibility criteria: Inclusion and exclusion criteria for this revieOnly randomized controlled trials (RCTs) will be eligible for inclusion regardless of the languages. It will not include animal experiments, case reports, non-clinical researches, commentaries, repeated publications, etc RCTs with incomplete and unavailable important data will be excluded. The study will include adult participants aged 18years or older who are definitely diagnosed with DKD according to Kidney Disease Outcomes Quality Initiative (KDOQI) criteria. There will be no restrictions on the type of DM, stage of the DKD, gender, nationality, race, education, and job. All intervention trails that meet inclusion criteria and include treatment with keluoxin capsule will be included. The control group could consist of any western medicine, placebo, or no intervention. Any herbals or Chinese medicine treatment will be excluded from the analysis.

Information sources: PubMed, Cochrane Library, EMBASE, China National Knowledge Infrastructure, WANFANG database, VIP, SinoMED, and Chinese Biomedical Literature Database (CBM) will be searched to ensure all possible RCT studies on keluoxin capsule, without limitation of the language.

Main outcome(s): The main outcome will be the mean change in albuminuria and eGFR.

Quality assessment / Risk of bias analysis: The methodological quality of the included studies and the risk of bias will be independently assessed by two reviewers using the risk of bias assessment tool from Cochrane Handbook. The sources of bias assessment will include selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other bias sources. Any disagreement will be resolved by the third reviewer.

Strategy of data synthesis: Random-effects model meta-analysis will be assessed using Revman software (version 5.3, Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration). The primary and secondary outcomes will be estimated as continuous outcomes evaluated by standard mean difference with 95% confidence interval (95% CIs), and dichotomous outcomes measured by odds

ratios with 95% CIs. The statistical heterogeneity between trial results will be conducted using a I2 statistic, and I2>50% will be considered to represent substantial heterogeneity. If I250%, the random effects model will be used. If the quantitative synthesis of data is not possible, qualitative analysis will be applied.

Subgroup analysis: Subgroup analysis will be conducted to investigate possible sources of heterogeneity across studies such as the stage of diabetic kidney disease, interventions, course of treatment, if sufficient data are available. To validate the robustness of meta-analytic estimates, we will remove each study in turn to observe the impact on the overall results to perform sensitivity analysis.

Sensitivity analysis: To validate the robustness of meta-analytic estimates, we will remove each study in turn to observe the impact on the overall results to perform sensitivity analysis.

Country(ies) involved: China.

Keywords: Keluoxin capsule; diabetic kidney disease(DKD); meta-analysis.

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