INPLASY

Efficacy of shenkang injection combined with renin-angiotensin-aldosterone system blockers in the treatment of diabetic nephropathy: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 September 2024 and was last updated on 10 September 2024.

INTRODUCTION

Review question / Objective The objective of this systematic review was to assess the efficacy of SKI combined with renin-angiotensin-aldosterone system (RAAS) blockers in treating DN by meta-analysis.

Condition being studied Diabetic nephropathy (DN) is a class of microvascular complications caused by diabetes mellitus. Previous studies have demonstrated that lowering urinary protein levels and controlling blood pressure can delay the progression of DN. The commonly used drugs in clinical practice are renin-angiotensin-aldosterone system (RAAS) blockers, especially angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), have shown promising results in the treatment of DN [4]. However, the use of RAAS blockers alone in reducing proteinuria in patients with massive proteinuria or reversing the pathological progression of DN remains challenging in clinical applications.

Shenkang injection (SKI) has been widely used in china for the treatment of diabetic nephropathy (DN). It is composed of 4 herbs, Salvia miltiorrhiza, Safflower, Rhubarb, and Radix Astragali, and is widely used in China for the treatment of kidney disease. Pharmacological studies have shown that Salvia miltiorrhiza and Safflower have anticoagulant, platelet aggregation inhibitory and vascular endothelial damage attenuating effects, while Rhubarb and Radix Astragali have anti-inflammatory and antioxidant effects. Basic studies have confirmed that SKI delays the progression of renal failure in DN mice and exerts renoprotective effects through different mechanisms of action, including enhanced antioxidant and anti-inflammatory activities as well

as amelioration of coagulation dysfunction. In addition, several clinical studies have demonstrated the significant effects of SKIs in the treatment of DN, such as lowering UAER, improving renal function, and having an improved hypercoagulable state . Therefore, SKIs have a clear role in improving DN, and a meta-analysis of the efficacy and safety of SKIs in combination with RAAS blockers is necessary.

METHODS

Participant or population Patients with a definite diagnosis of DN who meet the KDIGO (Kidney Disease: Improving Global Outcomes) 2020 Clinical Practice Guideline for Diabetes Management [14]. Patients will be of any age, gender, race, or clinical stage.

Intervention All of the literature used SKI combined with RAAS blockers and RAAS blockers along divided into two groups as interventions, regardless of dose, type or length of treatment. The basic therapies were similar between the combined treatment group and RAAS blocker group.

Comparator Literature is included that compares the efficacy and safety of SKIs in combination with RAAS blockers and RAAS blockers alone (ACEI or ARB) in the treatment of DN, irrespective of dose, type, or duration of treatment.

Study designs to be included Clinical randomised controlled trial.

Eligibility criteria The literature included in this study were randomised controlled trials (RCTs) with no restrictions on blinding or concealment of group allocation. There was no restriction on the type of literature, language or population characteristics.
Articles were excluded from the analysis for the following reasons: (1) Trials that do not meet predetermined inclusion criteria. (2) Studies using herbal preparations other than SKi. (3) Patients with other types of kidney disease. (4) Based on animal models or in vitro experiments, systematic reviews, conference papers. (5) Duplicate publications or articles with incomplete data.

Information sources We conducted a comprehensive search using the following databases: PubMed, Cochrane Library, Web of Science, Embase, CNKI, WanFang Data and VIP, for articles published between September 2004 and September 2024.

Main outcome(s) The primary outcomes were the total effective rate (TER), urinary protein excretion rate (UPER), urinary microprotein (β2-MG), and 24-h urinary protein levels (24 h UTP). Secondary outcomes comprised serum creatinine (Scr), blood urine nitrogen (BUN), fasting plasma glucose (FPG), and glycosylated hemoglobin (HbAlc).

Quality assessment / Risk of bias analysis Using the 'A revised tool to assess risk of bias in randomized trials (RoB 2) to assess research bias, including five steps: (1) randomization; (2) deviation from the intended interventions; (3) missing outcome data; (4) measurement of the outcome; (5) selection of the reported result [15]. The quality of each included literature was assessed according to the criteria of 'high risk of bias', 'low risk of bias' or 'some concerns'. The quality of evidence for each primary outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) . The assessment was performed using GRADEpro 3.6 software, which uses a four-item scale ('very low', 'low', 'moderate' or 'high ') to determine the risk of bias, inconsistency, indirectness and imprecision of the results, and the likelihood of publication bias. Risk of bias assessment and methodological quality were also assessed independently by two reviewers, and a third reviewer was consulted in case of discrepancies.

Strategy of data synthesis All data were analyzed using RevMan 5.3 and Stata 17.0. For dichotomous variables, we used relative risk (RR) and 95% confidence intervals (Cis). For continuous variables, we used weighted mean difference (WMD) or standardised mean difference (SMD), 95% confidence intervals (CI). Success rates (95% CI) and results of pooled analyses for each study are shown as forest plots. The degree of heterogeneity between studies was assessed using the I2 index. If no significant heterogeneity was observed (I2 0.05), a fixed effects model was used. Conversely, a random effects model was used. The weighting of the study was based on the DerSimonian and Laird stochastic models and is shown in the form of a forest plot. A funnel plot was used to represent the publication bias analysis, and the Egger test was added to quantify the extent of publication bias.

Subgroup analysis Subgroup analyses were also added to the basic analyses to determine the efficacy of the intervention in patients with different stages of DN.

Sensitivity analysis We performed sensitivity analyses by excluding each study in turn and comparing the results of the remaining studies to those of all studies. if the studies are all consistent, the finding is shown to be robust.

Country(ies) involved China.

Keywords Shenkang injection; RAAS blockers; traditional chinese medicine; diabetic nephropathy; meta-analysis.

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