INPLASY PROTOCOL

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None declared.

Effects of turmeric/curcumin on diabetic kidney disease: A meta-analysis of randomized controlled trials

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Review question / Objective: **Does turmeric/curcumin supplementation show effects on diabetic kidney disease?**
Condition being studied: **DKD is is one of the most common microvascular complications of diabetes mellitus (DM). According to the International Diabetes Federation, 463 million people worldwide were living with DM in 2019, which will rise to 700 million by 2045. Approximately 20% to 40% of patients with DM develop DKD. Patients with DKD have a higher risk of death with 3 to 12 times than those with DM alone. There has been a recent trend in the utilization of Curcumin supplements as an alternative or adjunct to conventional therapy. Turmeric/Curcumin is one of these supplements being utilized for its potential hypoglycemic, lipidlowering, anti-inflammatory and antioxidant effects in individuals with DKD.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 August 2021 and was last updated on 01 August 2021 (registration number INPLASY202180001).

INTRODUCTION

Review question / Objective: **Does turmeric/curcumin supplementation show effects on diabetic kidney disease?**

Rationale: **Diabetic kidney disease (DKD), a major cause of end-stage renal disease, has become a worldwide public health issue as a result of the increasing prevalence of diabetes. Patients with DKD are recommended to use renin-angiotensin-aldosterone system blockers, but many patients still progress to end-stage renal disease. Advances have been made in the treatment of DKD in recent years with the introduction of lifestyle changes, including exercise and diet, sodium-glucose cotransporter 2 inhibitors, and glucagon-like peptide-1 receptor.**

Unfortunately, these drugs were reported to have adverse effects, such as diabetic ketoacidosis and gastrointestinal, hinting the requirement for alternative and complementary therapy in the treatment of DKD. Turmeric, the dried extract from the rhizome of Curcuma longa, is extensively used in traditional medicine in Asian countries. Curcumin is the major active compound of turmeric and has attracted attention due to its its beneficial properties in treatment of diabetes and its complications due to its hypoglycemic, lipidlowering, anti-inflammatory and antioxidant effects.

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METHODS

Search strategy: ("Diabetic Nephropathies"[MeSH Terms] OR (("Glomerular Filtration Rate"[MeSH Terms] OR ("urinary albumin excretion rate"[Title/Abstract] OR "albumin excretion rate"[Title/Abstract] OR "albumin creatinine ratio"[Title/Abstract] OR "albumin to creatinine ratio"[Title/Abstract] OR "microalbuminuria"[Title/Abstract] OR "macroalbuminuria"[Title/Abstract] OR "creatinine clearance rate"[Title/Abstract] OR "serum creatinine"[Title/Abstract]) OR "Proteinuria"[MeSH Terms] OR "Albuminuria"[MeSH Terms] OR "Kidney Diseases"[MeSH Terms]) AND "Diabetes Mellitus"[MeSH Terms])) AND ("Curcumin"[MeSH Terms] OR "Curcuma*"[Title/Abstract] OR "zedoaria, Curcuma" [Title/Abstract] OR "Zedoar*" [Title/Abstract] OR "zedoaria, Zedoary" [Title/Abstract] OR "Curcuma longa*" [Title/Abstract] OR "longa, Curcuma" [Title/Abstract]OR "Tumeric*" [Title/Abstract]) AND (randomized controlled trial [Publication Type] OR controlled clinical trial [Publication Type] OR clinical trials [Title/Abstract] OR random* [Title/Abstract] OR trial[Title/Abstract]).

Participant or population: Diabetic kidney disease.

Intervention: Turmeric/Curcumin supplement.

Comparator: Placebo.

Study designs to be included: Randomized controlled trial.

Eligibility criteria: (1)Participants: Patients were diagnosed with DKD. No restrictions on the patients' sex, region, race, and disease course were implemented. (2) Interventions: The experimental group was administered turmeric/curcumin. (3) Comparion: the control group was treated with placebo. (3) Outcomes: reporting at least one of these outcomes: renal function: serum creatinine (SCr), estimated glomerular filtration rate (eGFR), blood urea nitrogen (BUN),proteinuria or albuminuria.; lipid: triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C); glycemic control: fasting blood-glucose (FBG), 2-hour post-meal blood glucose; bloodpressure. We excluded the studies if they met one of three criteria: (1) patients did not meet the diagnosis of DKD; (2) observational studies, cross-sectional, case reports, meta-analyses, animal experiments, or reviews.

Information sources: We will search the following electronic bibliographic databases: PubMed, Embase, Web of Science, Cochrane Library, Medline, and http://www.clinicaltrials.gov.

Main outcome(s): Renal function: serum creatinine (SCr), estimated glomerular filtration rate (eGFR), blood urea nitrogen (BUN),proteinuria or albuminuria.

Additional outcome(s): Lipid: triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol(HDL-C), low density lipoprotein cholesterol(LDL-C); glycemic control: fasting blood-glucose (FBG), 2-hour post-meal blood glucose; blood pressure.

Data management: Two reviewers will independently screen the initial search results through reading titles and abstracts to obtain potentially eligible studies. Next, they will retrieve the full-text of potentially eligible articles and check them against the inclusion criteria. A third reviewer will not take part in the discussion unless discrepancy. Then, the two reviewers will independently extract the following data using Microsoft Excel: basic information, participant characteristics, interventions, risks of bias, and available outcomes. For missing data, we will try our best to contact the corresponding authors by e-mail.

Quality assessment / Risk of bias analysis: Two reviewers will independently assess the risk of bias for all individual studies using the Cochrane Risk of Bias tool [Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0]. The following domains will evaluate: (1) selection bias including random sequence generation and allocation concealment, (2) performance bias including blinding of participants and personnel, (3) detection bias associated with blinding of outcome assessment, (4) attrition bias associated with incomplete outcome data, (5) reporting bias associated with selective reporting, and (6) other bias. We will judge the risk of bias as low, high, or unclear in each domain for each RCT. If there are discrepancies in two reviewers, it will be adjudicated by a third reviewer.

Strategy of data synthesis: We will compute effect size by weighted mean differences/ standard mean difference (for continuous outcomes) with 95% CI. Pooled estimates of the intervention effect will be calculated using a fixed effect model or a random-effects model meta-analysis for each outcome. Statistical heterogeneity will be evaluated by heterogeneity p-value and I^2 test. I^2 values of 25%, 50%, and 75% will be considered evidence of low-, moderate-, and high-heterogeneity respectively. If the heterogeneity is high, a subgroup analysis, sensitivity analysis, or meta- regression will be performed to identify the cause heterogeneity, and a random-effects model will used.

Subgroup analysis: If necessary, data are available, subgroup analyzes will be conducted based on mean age, duration of intervention, and turmeric/curcumin dosage.

Sensitivity analysis: The sensitivity analysis will be conducted to evaluate the stability of the results via omitting one study at a time and pooling the remaining ones.

Language: English.

Country(ies) involved: China.

Keywords: Diabetic kidney disease; turmeric; curcumin; randomized controlled trials; meta-analysis.

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