INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Effect of Traditional Chinese Medicine on Gut Microbiota with Chronic Kidney Disease: A Systematic Review and Meta-Analysis

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Review question / Objective: **The aim of this systematic review and meta-analysis was to assess the effects of TCM on renal function, modulation of gut microbiota ,andchanges of intestinal function in patients CKD.**
Information sources: **Seven electronic databases (Web of Science, PubMed, CNKI,Wanfang Database, CBM and VIP Information-Chinese Scientific Journal Database) were searched from inception to October 30, 2021 in the English and Chinese language.**
Main outcome(s): **The levels of biomarkers of renal function (serum creatinine [Scr] and blood urea nitrogen [BUN]; the modulation of gut microbiota (colibacillus, enterococcus, bifidobacterium and lactobacillus); the changes of intestinal function (D-lactate and endotoxin).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 October 2021 and was last updated on 30 October 2021 (registration number INPLASY2021100118).

INTRODUCTION

Review question / Objective: **The aim of this systematic review and meta-analysis was to assess the effects of TCM on renal function, modulation of gut microbiota, and changes of intestinal function in patients CKD.**

Condition being studied: **Effect of Traditional Chinese Medicine on Gut Microbiota with Chronic Kidney Disease. 1.The methodological quality and risk of bias (ROB) of all included studies were assessed by two authors (LH and XL) independently using the Cochrane Collaboration's tool. 2.We are funded, so we don't have to worry about the cost.**

METHODS

Participant or population: Adult patients (aged >18 years) diagnosed with CKD, including those who underwent hemodialysis, peritoneal dialysis, or did not undergo dialysis, regardless of gender, race and region.

Intervention: TCM interventions in the experimental group in the included studies consisted of Chinese herbal compounds, Chinese patent medicine, and single Chinese medical herbs, which can be administered in the form of decoctions, granules, or powders. Studies on herb extracts, TCM combined with any non-drug therapy, or TCM with other kinds of complementary and alternative medicine were excluded.

Comparator: Control: The control group included individuals that were treated with either Western medicine or placebo, or those that did not undergo any intervention. If TCM was combined with Western medicine in the experimental group, it was ensured that the use of Western medicine was consistent with that of the control group.

Study designs to be included: Study design: RCTs limited to Chinese or English.

Eligibility criteria: The inclusion criteria of the study were: (a)Study design: RCTs limited to Chinese or English; (b)Subjects: adult patients (aged >18 years) diagnosed with CKD, including those who underwent hemodialysis, peritoneal dialysis, or did not undergo dialysis, regardless of gender, race and region; (c)Interventions: TCM interventions in the experimental group in the included studies consisted of Chinese herbal compounds, Chinese patent medicine, and single Chinese medical herbs, which can be administered in the form of decoctions, granules, or powders. Studies on herb extracts, TCM combined with any non-drug therapy, or TCM with other kinds of complementary and alternative medicine were excluded;(d) Control: The control group included individuals that were treated with either Western medicine or placebo, or those that did not undergo any intervention. If TCM was combined with Western medicine in the experimental group, it was ensured that the use of Western medicine was consistent with that of the control group; (e) Outcomes: The levels of biomarkers of renal function (serum creatinine [Scr] and blood urea nitrogen [BUN]; the modulation of gut microbiota (colibacillus, enterococcus, bifidobacterium and lactobacillus); the changes of intestinal function (D-lactate and endotoxin). The exclusion criteria were: (a) study design: non-RCTs, such as retrospective studies, observational studies, case reports, and cross-over studies; (b)studies that could not be used for statistical analysis due to incomplete data; (c)repeated data studies; (d) reviews.

Information sources: Seven electronic databases (Web of Science, PubMed, CNKI, Wanfang Database, CBM and VIP Information-Chinese Scientific Journal Database) were searched from inception to October 30, 2021 in the English and Chinese language.

Main outcome(s): The levels of biomarkers of renal function (serum creatinine [Scr] and blood urea nitrogen [BUN]; the modulation of gut microbiota (colibacillus, enterococcus, bifidobacterium and lactobacillus); the changes of intestinal function (D-lactate and endotoxin).

Additional outcome(s): None.

Quality assessment / Risk of bias analysis: The risk of bias of the included RCTs in the aspects of randomization, allocation, and loss to follow-up were assessed following the Cochrane Handbook 5.3 for Systematic Reviews of Interventions. Each risk of bias item was rated as “Yes” (low risk of bias), “No” (high risk of bias), or “Unclear” (lack of relevant information or unclear risk of bias). The two reviewer (LH and XL) independently assessed the risk of bias in the included studies based on the following characteristics: randomized sequence generation, treatment allocation

concealment, blinding, completeness of outcome data, selective outcome reporting, and other sources of bias. Any disagreements between reviewers were resolved by consultation with a third reviewer(MC).

Strategy of data synthesis: Search results were merged into the reference management software Endnote (X9; Thomson Reuters). Two authors (LH and XH) manually and independently selected the relevant literature by screening titles and abstracts, and then assessed the full text based on the eligibility criteria using a study-selection form. Any disagreements were resolved via discussion with the third author (MC). The corresponding authors of the trials were contacted for clarification, if necessary.

Subgroup analysis: Review Manager 5.3, a systematic review software developed by the Cochrane Collaboration, was used for data analysis. In this study, the efficacy evaluation was a continuous variable, and because the outcome indicator measurement method and the outcome unit may be inconsistent, mean and SD of each study were obtained and pooled as mean difference (MD) or standardized mean differences (SMD) with a 95% confidence interval (CI). Considering the diversity of interventions and potential heterogeneity among included study, and to determine heterogeneity (P≥0.05 or I2≤50%= low heterogeneity, Fixed effect model; P<0.0.5 or I2 > 50% = random effect model, high heterogeneity or subgroup analysis).

Sensitivity analysis: Review Manager 5.3, a systematic review software developed by the Cochrane Collaboration, was used for data analysis. In this study, the efficacy evaluation was a continuous variable, and because the outcome indicator measurement method and the outcome unit may be inconsistent, mean and SD of each study were obtained and pooled as mean difference (MD) or standardized mean differences (SMD) with a 95% confidence interval (CI). Considering the diversity of interventions and potential heterogeneity among included study, and to determine heterogeneity (P≥0.05 or I2≤50%= low heterogeneity, Fixed effect model; P<0.0.5 or I2 > 50% = random effect model, high heterogeneity or subgroup analysis).

Country(ies) involved: China.

Keywords: CKD; Gut microbiota; Randomized controlled trials; Traditional Chinese medicine.

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