INPLASY PROTOCOL

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The authors have no conflicts of interest to disclose.

Effect of Chinese medicine prescription on nephrotic syndrome: A protocol for systematic review and meta-analysis

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Review question / Objective: **Investigate the clinical effect of traditional Chinese medicine prescriptions on nephrotic syndrome.**
Condition being studied: **Nephrotic syndrome (NS) is a large amount of proteinuria (urine protein greater than 3.5g / d), hypoalbuminemia (plasma albumin less than 30g / L), hyperlipidemia and varying degrees of edema (the first two of which Is necessary for diagnosis) is a syndrome with major clinical manifestations. The epidemiological status of nephrotic syndrome varies in different countries and regions. The average global incidence of nephrotic syndrome is 40.35%, with the highest rate in Iran (70%) and the lowest in Finland (16.4%). With the aging of the Chinese population, the incidence of nephrotic syndrome is also increasing, accounting for 42.2%. At present, western medicine treatment of nephrotic syndrome mainly uses glucocorticoids and immunosuppressants. Long-term application not only has large side effects, but also causes patients with low immune function and infection. In recent years, there have been many studies on the prescription of traditional Chinese medicine for the treatment of nephrotic syndrome. However, the sample size of these studies is not large and the quality of the studies is not the same. Therefore, we will conduct a meta-analysis of the effectiveness and safety of traditional Chinese medicine prescriptions to provide evidence-based evidence for the clinical treatment of nephrotic syndrome.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 April 2020 and was last updated on 26 April 2020 (registration number INPLASY202040181).

INTRODUCTION

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METHODS

Participant or population: Regardless of gender, age, ethnicity, education and economic status, patients with nephrotic syndrome who meet the following diagnostic criteria (e.g, Evidence-based clinical practice guidelines for nephrotic syndrome 2014) will be included.

Intervention: The intervention measures of the experimental group were oral traditional Chinese medicine prescriptions alone or traditional Chinese medicine prescriptions combined with conventional western medicine, regardless of the dosage form (tablets, mixtures, decoctions). The control group was treated with conventional western medicine, including hormones, immunosuppressive agents, diuretics, anti-platelet aggregation drugs, Chinese patent medicines, and dietary maintenance.

Comparator: The following treatment comparisons will be studied: 1. Oral traditional Chinese medicine prescription or traditional Chinese medicine combined with conventional western medicine compared with conventional western medicine; 2. Oral traditional Chinese medicine prescription or traditional Chinese medicine combined with conventional western medicine compared with placebo; 3. Comparison of oral traditional Chinese medicine prescription or traditional Chinese medicine prescription combined with conventional western medicine and other effective therapies; We will evaluate and compare traditional Chinese medicine prescription therapies based on the training and education methods of doctors, their clinical experience, the total number of treatments, the time and frequency of treatment.

Study designs to be included: Inclusion: randomized controlled trials (RCTs), without limitations on language or publication status. Exclusion: animal studies, case reports, self-.

Eligibility criteria: Meet the following diagnostic criteria (e.g, Evidence-based clinical practice guidelines for nephrotic syndrome 2014).

Information sources: We will search electronically and manually for all RCTs that treat traditional Chinese medicine prescriptions for nephrotic syndrome, regardless of publication status and language, up to February 2020. The databases to be searched will include: PubMed, EMBASE, Springer, Web of Science, the Cochrane Library, WHO International Clinical Trials Registry Platform (ICTRP), Traditional Chinese Medicine databases (TCMD), China National Knowledge Infrastructure (CNKI), China Biomedical Literature Database (CBM), Chinese Scientific Journal Database (VIP) and Wan-Fang database. In addition, the reference lists of identified publications, and various meeting minutes,

will also be screened for further material, and a manual search of the grey literature, including unpublished conference articles, will also be undertaken.

Main outcome(s): After at least two weeks of treatment, evaluate the effect of Chinese medicine prescriptions on nephrotic syndrome using total clinical efficacy rate or other validated scales.

Additional outcome(s): 24-hour urine protein quantification, blood urea nitrogen (BUN), serum creatinine (Scr), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), and interleukin 6 (IL-6). Recurrence rates and adverse events during follow-up.

Data management: Prior to the literature search, researchers (Yuanshu Ou) will be trained to ensure consistency in the evaluation of this study. During the literature screening, we will use EndNote X8 document management software. The two reviewauthors (YLDandLXZ) will strictly adhere to the inclusion criteria and will independently filter all studiesretrieved from the search based on their title, abstract, and keywords to determine eligible studies. We will then obtain the full text of all studies that are potentially relevant for further evaluation. If there is a disagreement during the screening process, it will be discussed by two authors (YLDandLXZ) and a third author (Yuanshu Ou) and arbitration will be conducted if necessary. Excluded studies will be recorded and explained, and if necessary, we will contact the trial authors to clarify any unclear information. For duplicate publications, we only select the original text. The following information will then be extracted from the selected studies: general information, methods of participation, interventions, results, outcomes, adverse events, conflicts of interest, ethical recognition and any other relevant information.

Quality assessment / Risk of bias analysis: The authors (AWW and DXX) will use the Cochrane Collaboration's bias risk assessment tool to assess the risk of bias in all included studies. We will assess the risk of bias in the following areas: sequence generation, assignment sequence hiding, blindness of participants and staff, and result evaluators, incomplete outcome data, selective outcome reporting, and other sources of bias. We will use L, U, and H to rate the assessments, with L (low) indicating a low risk of bias, U (unclear) indicating an uncertain risk of bias, and H (high) indicating a high risk of bias. All reviewers will resolve any differences through discussion. Information on the risk of bias assessments included in the review will be summarized in tabular form, and the results and impacts will be critically discussed. If the information is found to be ambiguous, we will try to contact the author concerned.

Strategy of data synthesis: Data analysis and a quantitative data synthesis will be performed using RevMan V.5.3. For continuous data, if there is no heterogeneity, we will use mean difference (MD) or standard MD (SMD) to measure the therapeutic effect of 95% CIs. If significant heterogeneity is found, a random effects model will be used. For dichotomous data, we will use 95% CI hazard ratios (RR) for the analysis (heterogeneity will be texted as described below). We will include data from parallel group design studies for the meta-analysis, and only the first phase of the data will be included in random crossover trials. In these trials, participants will be randomly divided into two intervention groups, and individual measurements for each outcome for each participant will be collected and analyzed. The results will be expressed as the RR of the binary data and the SMD of the continuous data. Heterogeneity levels will be tested using the I^2 statistic, and for values less than 50%, a fixed effect model will be used for the data synthesis, whereas if I^2 is between 50% and 75%, a random effects model will be used instead. If I^2 results exceed 75%, we will investigate the possible causes from a clinical and methodological perspective and provide a descriptive analysis or a subgroup analysis.

Subgroup analysis: Despite the information, there is no plan, but factors such as nephrotic syndrome subgroups and traditional Chinese medicine prescriptions will be considered. In addition, if significant heterogeneity is found, we will perform subgroup analyses as appropriate.

Sensibility analysis: To test the robustness of the review conclusions, a sensitivity analysis will be performed for the primary outcome according to the following criteria: sample size, heterogeneity quality, and statistical model (random-effects or fixed-effects model). The results will be compared and discussed.

Language: No limit.

Country(ies) involved: China.

Keywords: Chinese medicine prescription, nephrotic syndrome, systematic review protocol.