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Clinical Efficacy of Chinese patent medicines combined with standard drug treatment for treatment of lupus nephritis in Adults: A Multiple-Treatment Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 February 2025 and was last updated on 11 February 2025.

INTRODUCTION

Review question / Objective Combinations of Chinese patent medicines (CPMs) with Standard drug treatments (SDT) (including glucocorticoids, hydroxychloroquine, immunosuppressants, and biological agents) are frequently utilised in the treatment of lupus nephritis in adults. However, the efficacy of these combination treatments remains to be established.

Condition being studied Lupus nephritis (LN) is one of the most common and serious complications of systemic lupus erythematosus (SLE) and a major cause of death in SLE patients, with kidney involvement occurring in 40% to 60% of SLE patients. Lupus nephritis (LN) is mainly caused by renal injury due to circulating or in situ immune complex deposition, whereas a small proportion of patients with systemic lupus erythematosus (SLE) suffer from renal injury via non-immune complex pathways (e.g., lupus interstitial nephritis) or renal vascular lesions.With in-depth research on the molecular mechanisms of LN, the emergence of therapeutic agents and treatments targeting specific pathogenic targets, and the widespread use of conventional therapeutic regimens such as steroids and immunosuppressants in patients with LN, the survival rate of patients with LN has improved significantly over the past two decades, but 14% to 33% of patients are still ineffective on first-line drugs or cannot tolerate the complications and adverse effects of treatment, which ultimately However, 14% to 33% of patients are still ineffective or unable to tolerate the complications and adverse effects of the first-line drugs, which eventually lead to the deterioration of renal function and end stage kidney disease (ESKD).
Chinese patent medicines (CPMs) have been shown to improve LN, reduce hormone use, mitigate the toxic side effects of immunosuppressants, and improve quality of life (QoL) (Dai et al. 2020; Wang et al. 2021; Chen et al.

2023; Ma et al. 2016). Chinese proprietary medicines (CPMs) are ready-to-use medicines made from Chinese botanicals and formulated according to specific therapeutic principles, which are characterized by multi-components and multi-targets.CPMs are processed according to prescription and compounding methods under the guidance of Chinese medicine theories and according to the needs of disease prevention/treatment (Zhang et al., 2024; Li et al., 2024). Studies have shown that CPM adjunct to standard medication is more effective than standard medication alone for adults with LN. (Dai et al. 2020; Wang et al. 2021; Chen et al. 2023; Ma et al. 2016). However, the optimal combination of CPM combined with standard drug therapy (SDT) for the treatment of LN has not been fully characterized, which poses a challenge for clinicians and patients when choosing a treatment. Therefore, we conducted a multiple treatment meta-analysis (MTMA). In this regard, a systematic analysis of previous research results using a multiple treatment meta-analysis method that integrates direct and indirect evidence is urgently needed to provide clinicians with both timely and scientific references to help them make more accurate and rational therapeutic decisions when formulating treatment strategies for lupus nephritis.

METHODS

Search strategy We conducted electronic searches across several databases: PubMed, MEDLINE, Scopus, Web of Science, Cochrane, Embase, China National Knowledge Infrastructure, Science and Technology Journal Database, and Wanfang. Our searches covered the period from the inception of these databases up toJanuary 2025 . Manual searches were also performed, and the authors of the original publications were contacted via email for additional data or clarification when necessary; however, most did not respond and were subsequently excluded.

Participant or population Participants aged 18 years or older (regardless of sex, ethnicity, region, or nationality) were eligible when they had a primary diagnosis of lupus nephritis (LN) in accordance with the guidelines.

Intervention In the context of evidence – based medicine for lupus nephritis (LN) treatment, trials examining the combination of Chinese patent medicine (CPM) and standard pharmacotherapy (SDT) were included. Standard pharmacotherapy (SDT), as defined in current clinical guidelines, consists of glucocorticoids, hydroxychloroquine, immunosuppressants, and biological agents. These agents are commonly used to control inflammation, suppress the immune system, and improve renal function in LN patients. In contrast, trials incorporating herbal remedies with CPM were excluded, as the quality and standardization of herbal medicines may vary widely, which could introduce confounding factors to the study results.

Comparator The control group was composed of trials that used only SDT as a pharmacological intervention, while the experimental group used a combination of CPMs in addition to the SDT used in the control group.

Study designs to be included The trial outcomes encompassed randomized controlled trials (RCTs) related to clinical efficacy.

Eligibility criteria The trial outcomes encompassed randomized controlled trials (RCTs) related to clinical efficacy, urinary protein quantification, serum creatinine (SCr), and the Systemic Lupus Erythematosus Disease Activity Score (SLEDAI).Fifth, the included studies were RCTs published in journals, with no language restrictions (either English or Chinese). Conference papers, reviews, or studies with incomplete data were excluded. In cases where data from the same study were published in multiple articles at different times, we selected the most recent publication.

Information sources We conducted electronic searches across several databases: PubMed, MEDLINE, Scopus, Web of Science, Cochrane, Embase, China National Knowledge Infrastructure, Science and Technology Journal Database, and Wanfang. Our searches covered the period from the inception of these databases up toJanuary 2025 . Manual searches were also performed, and the authors of the original publications were contacted via email for additional data or clarification when necessary; however, most did not respond and were subsequently excluded.Conference papers, reviews, or studies with incomplete data were excluded. In cases where data from the same study were published in multiple articles at different times, we selected the most recent publication.

Main outcome(s) The primary outcomes were as follows:(I) Complete renal remission rate: normal urine protein (urine protein quantification < 0.5g/24h or urine protein/creatinine ratio 50% decrease in urine protein from baseline, quantitative urine protein 30g/L, Scr increase ≤ 10% of baseline.(III) Assessment of SLE symptom change from baseline to post – intervention by SLEDAI

score.The secondary outcome was post – intervention urine protein level change. When multiple measures were used, priority was given to objectively – assessed outcomes by healthcare professionals.

Data management Two reviewers (MW, AJL) independently conducted data extraction. Using a standardized form, they collected the following information for each article:(1) Study details: sample size, participants' mean age, mean illness duration, sex distribution, and baseline participant characteristics.(2) Intervention specifics: dosage and regimen of CPM.(3) Methodological aspects: bias-risk assessment and diagnostic tools. A third researcher was on standby to resolve any disagreements.

Quality assessment / Risk of bias analysis Two authors (MW and AJL) independently assessed the overall bias risk of selected studies using the 2019-revised Cochrane Risk of Bias Tool (RoB2) (Sterne et al., 2019). Meanwhile, two other authors (CJL and XHL) independently evaluated the evidence certainty via the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach (Guyatt et al., 2011; Granholm et al., 2019).

Strategy of data synthesis To compare all adjunctive interventions, we performed a Multiple Treatment Meta – analysis (MTMA) using R 4.3.5 (R Institute of Statistical Computing, Vienna, Austria) and Stata MP17 (www.stata.com/) (Watt et al., 2019, 2022). We chose the random-effects model to account for expected heterogeneity.For various numerical outcomes, we used effect – size indicators such as relative risk (RR), standardized mean difference (SMD), and 95% confidence interval (CI). The MTMA was conducted on an intention – to – treat basis, with $p < 0.05$ (two-sided) indicating significance.We employed linear meta – regression analyses to explore potential moderators of Chinese patent medicine (CPM) combined with standard drug therapy (SDT) for lupus nephritis (LN). Publication bias was assessed via visual inspection of funnel plots.We utilized the surface under the cumulative ranking curve (SUCRA) and probability to rank the outcomes of each CPM as an adjunct to SDT in treating adult LN patients (Watt et al., 2019, 2022). Additionally, clustering analysis was used to compare interventions with two outcome indicators, facilitating better outcome selection.

Subgroup analysis No.

Sensitivity analysis No.

Language restriction No.

Country(ies) involved China.

Keywords multiple-treatments meta-analysis, standard drug treatment ,Chinese patent medicines , Lupus nephritis , Combined therapy.

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