INPLASY

Dual-Pathway Antifibrotic Strategies: Network Meta-Analysis of Herbal and Synthetic Drugs Inhibiting Mesothelial EMT in Rodent Peritoneal Fibrosis Models

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data extraction.

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 23 March 2025 and was last updated on 23 March 2025.

INTRODUCTION

Review question / Objective The primary objective of this study is to employ a network meta-analysis (NMA) framework to systematically elucidate the therapeutic efficacy of active compounds derived from herbal sources and synthetic drugs in rodent models of peritoneal fibrosis (PF). This investigation aims to generate methodologically rigorous comparative evidence to inform targeted pharmacotherapeutic interventions against peritoneal fibrosis, thereby facilitating clinical translation for improving prognosis in peritoneal dialysis (PD) patients through high-grade evidence-based medical decision-making.

Rationale PF represents one of the most severe complications of long-term PD, characterized by progressive structural and functional alterations in the peritoneal membrane. This pathophysiological process compromises ultrafiltration and constitutes a major risk factor for dialysis withdrawal. Current preclinical studies have demonstrated promising therapeutic effects of both herbal active compounds and synthetic drugs on animal models of peritoneal fibrosis. However, clinical translation studies of these drugs remain unreported. Therefore, we conducted a NMA to systematically evaluate their actual therapeutic efficacy.

Condition being studied Peritoneal dialysis is frequently used as a renal replacement therapy for patients with end-stage renal disease (ESRD). However, conventional high-glucose dialysate remains extensively utilized in clinical practice, which necessitates heightened scientific attention to their propensity for inducing PF through glucose degradation products (GDPs) and advanced glycation end products (AGEs). Epithelial-mesenchymal transition (EMT) in mesothelial cells is essential for the progression of peritoneal fibrosis. To date, no specific drug treatments for PF through suppression of EMT are available. Nevertheless, several anti-fibrotic herbal active compounds and synthetic agents have demonstrated therapeutic efficacy in preclinical

studies, suggesting their potential applicability as targeted interventions for EMT to prevent PF.

METHODS

Search strategy We searched the Cochrane Library, Embase, PubMed, Scopus, and Web of Science databases from inception to the end of March, 2024, using the following search terms: (Epithelial-Mesenchymal Transition OR Epithelial Mesenchymal Transition OR EMT OR mesothelial-mesenchymal transition OR mesothelial mesenchymal transition OR MMT) AND (peritoneal fibrosis OR PF OR peritoneal sclerosis OR encapsulating peritoneal sclerosis OR sclerosing peritonitis).

Participant or population Various types of PD-associated peritoneal fibrosis of mice or rats.

Intervention Inclusion criteria: the experimental group comprises rodent PF models treated with intragastrically administered herbal active compounds or synthetic agents. Exclusion criteria: (1) rodent PF models treated with inhibitors via any mode of drug delivery; (2) rodent models of PF receiving intraperitoneal or intravenous injection of herbal active compounds or synthetic agents.

Comparator Rodent models of PF treated with placebo, distilled water or saline.

Study designs to be included Control studies are included.

Eligibility criteria (1) studies involving rodent models of PF; (2) studies involving herbal active compounds or synthetic drugs inhibiting mesothelial EMT in rodent peritoneal fibrosis models; (3) study outcomes involving peritoneal function, inflammation factors, MMT and fibrotic markers.

Information sources Online databases (Cochrane Library, Embase, PubMed, Scopus, and Web of Science databases).

Main outcome(s) Our study focuses on the analysis of peritoneal function, inflammation factors, MMT and fibrotic markers.

Additional outcome(s) Other histological and molecular changes.

Quality assessment / Risk of bias analysis Two independent reviewers assess the quality of each included studies using SYRCLE Animal Experiment Bias Risk Assessment, which including: (1) sequence generation; (2) baseline characteristics; (3) allocation concealment; (4) random housing; (5) researchers blinding; (6) random outcome assessment; (7) outcome assessors blinding; (8) complete outcome data; (9) outcome reporting; and (10) other source of bias. A difference in opinions will be decided by the third reviewer. The final results are imported into Reveman software to generate a risk of bias map.

Strategy of data synthesis For continuous variables in this study, network meta-analysis (NMA) is conducted using STATA software, with standardized mean difference (SMD) employed as the effect measure. All effect estimates are reported with 95% confidence intervals (CI), and statistical significance is determined when the 95% CI of the effect measure does not cross the null effect line. The intervention effects are ranked using the Surface Under the Cumulative Ranking curve (SUCRA). Publication bias and small-sample effects are assessed by funnel plots.

Subgroup analysis There is no subgroup analysis.

Sensitivity analysis Stata software was employed to conduct leave-one-out sensitivity analysis, whereby the robustness of pooled estimates was evaluated by systematically examining effect size variations subsequent to the sequential exclusion of individual studies.

Country(ies) involved China.

Keywords Herbal medicine; EMT; Peritoneal fibrosis.

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