INPLASY PROTOCOL

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None declared.

Comparative Efficacy and safety of Various CPMs Combined with Western Medicine for adults with Insomnia : A Bayesian Network Meta-Analysis of Randomized Controlled Trials

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Review question / Objective: **Given the limitations of Western medicine (WM) for the treatment of adults with Insomnia and the wide exploration of Chinese patent medicines (CPMs) , systematically evaluate the efficacy and safety of Various CPMs Combined with WM for adults with Insomnia. In this study, we performed a network meta-analysis to evaluate the comparative efficacy and safety of 16 CPMs combined with WM regimens for the treatment of adults with Insomnia.**
Condition being studied: **Given the limitations of Western medicine (WM) for the treatment of adults with Insomnia and the wide exploration of Chinese patent medicines (CPMs) , systematically evaluate the efficacy and safety of Various CPMs Combined with WM for adults with Insomnia.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 January 2023 and was last updated on 11 January 2023 (registration number INPLASY202310030).

INTRODUCTION

Review question / Objective: **Given the limitations of Western medicine (WM) for the treatment of adults with Insomnia and the wide exploration of Chinese patent medicines (CPMs) , systematically evaluate the efficacy and safety of Various CPMs Combined with WM for adults with Insomnia. In this study, we performed a network meta-analysis to evaluate the comparative efficacy and safety of 16 CPMs combined with WM regimens for the treatment of adults with Insomnia.**

Rationale: **In this study, we performed a network meta-analysis to evaluate the comparative efficacy and safety of 16 CPMs combined with WM regimens for the treatment of adults with Insomnia.**

Condition being studied: Given the limitations of Western medicine (WM) for the treatment of adults with Insomnia and the wide exploration of Chinese patent medicines (CPMs) , systematically evaluate the efficacy and safety of Various CPMs Combined with WM for adults with Insomnia.

METHODS

Search strategy: Literature databases were searched from their inception to November 2022, and all randomized control trials (RCTs) involving adults with Insomnia patients treated with a combination of Chinese patent medicines and WM were retrieved.

Participant or population: According to the standard operational diagnostic criteria (Feighner criteria, Figner criteria, DSM-III, DSM-III-IIR, DSM-IV, DSM-5 and ICD-10) (Rosen et al., 2021; Davies et al., 2017; Möller et al., 2018), adults (≥ 18 years old, male and female) were initially diagnosed Insomnia.There were no limitations on sex, race, region or nationality.

Intervention: Patients in the treatment group received CMPs together with WM therapy.

Comparator: Patients in control groups received only WM regimens, including Benzenediazepines (BZDs), Z-drugs, Melatonin, H1antagonists, Orexin receptor antagonists (ORAs), Antipsychotics and Antidepressants.

Study designs to be included: RCTs that reported the efficacy and safety of the 16 CMPs combined with WM for treating adults with Insomnia were eligible. There were no language restrictions. When outcome information was available for multiple time points, the data for the longest follow-up time point were selected.

Eligibility criteria: The exclusion criteria were as follows: 1) Other traditional Chinese Medicine treatment options (Chinese herbal injections (CHIs), emotional therapy, static breathing control, acupuncture); 2) repeat publications; and 3) Studies with incomplete or incorrect data ; 4) Study without one of the above outcome indicators; 5) Cognitive behavioral therapy (CBT-I).

Information sources: A computerized search of Chinese Biological Medicine Literature, China National Knowledge Infrastructure(CNKI),the China Science and Technology Journal database (VIP), Wanfang, PubMed, Cochrane Library, and Embase databases for literatures on RCTs of CPMs combined with WM regimens for the treatment adults with Insomnia was performed up to November, 2022. At the same time, manually retrieve the relevant meta-analysis of Chinese patent medicine combined with western medicine in the treatment of insomnia, and screen its references. The search strategy was divided into three parts: CMPs, Insomnia, and RCTs.

Main outcome(s): The Effectiveness outcome indicator was total effective, where total effective was defined as Cure+markedly effective+effective. Sleep quality was assessed using the Pittsburgh sleep quality index (PSQI). Security outcome indicators were the incidence of somnolence, incidence of dry mouth, incidence of dizziness. Data were extracted according to the predefined definitions described in the protocol, with priority given to the earliest published report when data appeared in more than one report. In this study, at least one outcome measure was included in randomized controlled trials.

Quality assessment / Risk of bias analysis: Two researchers (Jianhe Li and Wei Cui) independently assessed the risk of bias in included RCTs according to the risk of bias tool provided in the Cochrane Handbook for Systematic Reviews of Interventions. The following were assessed: (1) selection bias associated with random sequence generation; (2) selection bias associated with allocation concealment; (3) performance bias: blinding of participants and personnel; (4) detection bias: blinding of outcome assessments; (5) attrition bias:

completeness of outcome data; (6) reporting bias: selective reporting; and (7) other sources of bias. Each factor was categorized as "low risk", “high risk”, or "unclear". All discrepancies that emerged from this study were discussed by a review panel.

Strategy of data synthesis: For the research published many times (i.e. repeated research), we only include the report with the richest information and the most complete data. We used Bayesian network element analysis to estimate the summary odds ratio (ORs) of dichotomous results and the standardized mean difference (SMD, Cohen's d) of consecutive results. All meta-analyses were performed using R4.2.1 software for statistical analysis of data and research, and a Markov chain Monte Carlo method for Bayesian inference. The parameters set in R4.2.1 software were as follows: number of chains, 4; tuning iterations, 20,000; simulation iterations, 100,000; thinning interval, 1; settings of tuning iterations and simulation iterations were adjusted according to the actual situation. Potential scale reduction factors were used to evaluate the convergence of Markov chains. Models were compared using the deviance information criterion, which is equal to the sum of the posterior mean of the residual deviations and the number of valid parameters. Network diagrams showing indirect comparative relationships among different interventions were generated, where the nodal areas for each intervention represent the number of patients, and the thickness of lines between different interventions represented the number of RCTs.We used R4.2.1 and Stata MP17 software to plot cumulative probability ranking and to generate mesh and funnel plots . In order to estimate the probability of ranking each intervention, the surface under the cumulative ranking area (SUCRA) curve is used; the larger the area under the curve, the higher the ranking and the higher the probability that the CMPs are the best interventions (Salanti et al., 2011). Clustering analysis was used to synthesize and compare interventions with two different outcome indicators, in order to obtain the best choice of two result indicators: the farther away from the origin in the cluster graph, the better the result indicators. Acomparison-adjusted funnel plot was used to assess potential publication bias. If points on both sides of the midline in the funnel diagram were symmetric, which meant the correction guideline was at right angles to the midline, it was considered indicative of no significant publication bias (Sterne et al., 2011; Lin et al., 2019; Lin et al.,2018).

Subgroup analysis: No.

Sensitivity analysis: No.

Country(ies) involved: China.

Keywords: network meta-analysis, Bayesian model, Chinese patent medicines, adults with Insomnia , Combined therapy, Chinese medicine.

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