INPLASY PROTOCOL

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Review Stage at time of this submission: The review has not yet started.

Conflicts of interest:
None declared.

The efficiency observation in a combination therapy with acupuncture and Chinese herbal medicine for insomnia

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Review question / Objective: The purpose of this study is to evaluate the safety and effectiveness of acupuncture combined with traditional Chinese medicine in the treatment of insomnia, and to provide basis for clinical decision-making.

Information sources: The following databases will be searched from their inception to May 2022: Web of Science, the Cochrane Library, PubMed, Embase, China biomedical literature database（CBM）, China National Knowledge Infrastructure（CNKI）, Chinese Scientific Journals Database (VIP), and the WanFang Database. We will also manually search for unpublished studies and references.We will search for ongoing or unpublished studies from ClinicalTrials. gov, China Clinical Trials Registry, PROSPERO, National Institutes of Health Registry, and World Health Organization International Clinical Trials Registry. Manually retrieve any potential gray Literature, search for a list of related references for additional trials. We will contact experts and authors in the field to learn about their progress and obtain important information that cannot be found in the search.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 May 2022 and was last updated on 13 May 2022 (registration number INPLASY202250082).

INTRODUCTION

Review question / Objective: The purpose of this study is to evaluate the safety and effectiveness of acupuncture combined with traditional Chinese medicine in the treatment of insomnia, and to provide basis for clinical decision-making.

Rationale: We will search the following 8 databases from their inception to May 2022: Web of Science, the Cochrane

Library, PubMed, Embase, Chinese Biomedicine, China National Knowledge Infrastructure, Chinese Scientific Journals Database, and the WanFang Database . All relevant randomized controlled trials (RCTs) were imported into EndNote 20 software for management, and RevMan V5.4.1 software was used for data analysis.

Condition being studied: Insomnia is a disease characterized by nocturnal sleep disorder and affected daytime function. The clinical manifestations are difficulty falling asleep, difficulty in sleep maintenance and dissatisfaction with sleep quality, which can be accompanied by daytime fatigue, depression or anxiety, physical discomfort, inattention, memory decline and cognitive impairment. According to epidemiological studies, insomniacs account for about 10%-30% of the total population. Female are higher than male, and the incidence rate of the elderly population is higher. In recent years, with the acceleration of people's pace of life and the increase of pressure, its incidence rate has increased year by year and tends to be younger. Western medicine often adopts drug therapy to treat insomnia, which has positive short-term effects in the treatment of insomnia, but there are potential risks such as adverse reactions, addiction and withdrawal symptoms in long-term use. Non-drug therapy needs to be carried out under the guidance of psychotherapists for a long time, which is a burden of both time and money for patients. Long-term use of drug treatment side effects are serious, non-drug treatment effect is not ideal, more and more insomnia patients are seeking alternative therapy.As one of the complementary and alternative therapies for insomnia, traditional Chinese medicine (TCM) has been increasingly applied in the treatment of insomnia, especially acupuncture and Chinese herbal therapy, and has achieved good clinical effects. Under the guidance of TCM syndrome differentiation theory, acupuncture and traditional Chinese medicine have the function of regulating the neuro-humoral-immune system of insomniacs, and have the characteristics of precise curative effect and fewer side effects in improving

symptoms and sleep quality of insomniacs. However, as a traditional treatment technology, the biggest problem of acupuncture and traditional Chinese medicine in the treatment of insomnia is the lack of scientific clinical efficacy certification and safety evaluation. At present, there is no systematic review of acupuncture plus Chinese herbal medicine in the treatment of insomnia. In order to confirm whether acupuncture and Chinese herbal medicine in the treatment of insomnia is real and effective, evidence-based medicine should be adopted to summarize and analyze data in high-quality randomized controlled trials (RCTs), and evaluate its effectiveness and safety, so as to provide evidence for clinical decision-making.

METHODS

Search strategy: The following databases will be searched from their inception to May 2022: Web of Science, the Cochrane Library, PubMed, Embase, China biomedical literature database (CBM) , China National Knowledge Infrastructure (CNKI) , Chinese Scientific Journals Database (VIP) , and the WanFang Database. We will also manually search for unpublished studies and references. The search strategy for the PubMed is presented in Table 1, Other database retrieval strategies will be dynamically adjusted to suit the corresponding database retrieval requirements. Chinese databases will be searched by Chinese characters with synonym items.

Participant or population: The patients included in study should be the one who have been clearly diagnosed with insomnia, the diagnosis of insomnia is confirmed by comprehensive consultation and scale assessment. Regardless of gender, nationality, race, education or severity of disease.

Intervention: The experimental group received acupuncture related plus Chinese herbal medicine therapies (including body acupuncture, scalp acupuncture, electric

acupuncture, ear acupuncture, fire acupuncture, warm acupuncture, fast acupuncture, skin acupuncture, moxibustion, cupping, blood pricking, acupoint catgut embedding, Chinese herbal medicine).

Comparator: The control group received conventional symptomatic treatment, placebo acupuncture, western medicine.

Study designs to be included: A comprehensive search was conducted for randomized controlled trials of acupuncture combined with Chinese medicine in the treatment of insomnia. The language is limited to Chinese or English. Reviews, case reports, mechanism studies, data mining, expert clinical experience, non-randomized controlled trials were excluded.

Eligibility criteria: 1.Types of studies. A comprehensive search was conducted for randomized controlled trials of acupuncture combined with Chinese medicine in the treatment of insomnia. The language is limited to Chinese or English. Reviews, case reports, mechanism studies, data mining, expert clinical experience, non-randomized controlled trials were excluded.2.Types of participants. The patients included in study should be the one who have been clearly diagnosed with insomnia, the diagnosis of insomnia is confirmed by comprehensive consultation and scale assessment. Regardless of gender, nationality, race, education or severity of disease.3. Interventions and comparisons. The experimental group received acupuncture related plus Chinese herbal medicine therapies (including body acupuncture, scalp acupuncture, electric acupuncture, ear acupuncture, fire acupuncture, warm acupuncture, fast acupuncture, skin acupuncture, moxibustion, cupping, blood pricking, acupoint catgut embedding, Chinese herbal medicine) . The control group received conventional symptomatic treatment, placebo acupuncture, western

medicine.4. Outcomes. (1) Primary outcomes. One course of treatment (1 month), to determine the efficacy. Sleep efficiency was the primary outcome of insomnia. (2) Secondary outcomes. We will also focus on the following indexes: Insomnia Severity Index (ISI); Pittsburgh Sleep Quality Index (PSQI); Self-Rating Anxiety Scale (SAS). In addition, we also pay attention on the adverse reactions of patients during treatment period.

Information sources: The following databases will be searched from their inception to May 2022: Web of Science, the Cochrane Library, PubMed, Embase, China biomedical literature database（CBM）, China National Knowledge Infrastructure（CNKI）, Chinese Scientific Journals Database（VIP）, and the WanFang Database. We will also manually search for unpublished studies and references.We will search for ongoing or unpublished studies from ClinicalTrials. gov, China Clinical Trials Registry, PROSPERO, National Institutes of Health Registry, and World Health Organization International Clinical Trials Registry. Manually retrieve any potential gray Literature, search for a list of related references for additional trials. We will contact experts and authors in the field to learn about their progress and obtain important information that cannot be found in the search.

Main outcome(s): One course of treatment (1 month), to determine the efficacy. Sleep efficiency was the primary outcome of insomnia.

Additional outcome(s): We will also focus on the following indexes: Insomnia Severity Index (ISI); Pittsburgh Sleep Quality Index (PSQI); Self-Rating Anxiety Scale (SAS). In addition, we also pay attention on the adverse reactions of patients during treatment period.

Data management: Endnote 20 was used to manage the collected literature, and duplicate articles were initially screened for exclusion. Two researchers (ZCW and JXL) will review the search results against the

criteria. They will independently review the titles and abstracts of literature to exclude studies that do not meet the requirements. Any problem in the process of literature screening will be solved by two researchers through consultation. If there is no consensus, the third researcher (JLW) will be involved until the consensus is reached. The data will be extracted independently by two researchers (ZCW and JXL) and recorded into Microsoft 365 Excel. Any disputes shall be negotiated with a third party (JLW) to resolve differences in data extraction. The extracted content included the first author, the year of publication, study type, sample size, age, characteristics of participants, Intervention measures of the treatment group and the control group and outcome indicators.

Quality assessment / Risk of bias analysis: We will use the Grading of Recommendations Assessment approach to assess the overall quality of evidence supporting the primary outcomes. There are 4 levels of evidence: very low, low, medium or high. To assess potential publication bias, if more than 10 studies were included, a funnel plot was plotted using Revman V5.4.1 to test for potential publication bias.

Strategy of data synthesis: Meta-analysis of included outcome data will be conducted using RevMan V.5.4.1, and we will select dichotomy results or continuous results according to different data types. Relative risk or odds ratio (95% confidence interval) is used for dichotomy results, while mean difference or standard mean difference (95% confidence interval) is used for continuous results. According to the results of heterogeneity test, random or fixed effect models will be selected for data statistics. The specific methods are as follows: If the heterogeneity was low ($P > .05$ or $I2 < 50\%$), the fixed-effect model is used for data synthesis; If heterogeneity was high ($P < .05$ or $I2 > 50\%$), data is synthesized using a random-effects model after possible sources of heterogeneity were excluded. If data cannot be synthesized, we provide a descriptive analysis to solve this problem.

Subgroup analysis: If there is significant heterogeneity between the results, a subgroup analysis will be performed to explore the cause.

Sensitivity analysis: Sensitive analysis will be performed to evaluate the robustness of the meta-analysis results. We observed the stability of individual studies on the whole by deleting them one by one. If no qualitative change occurs, the result is considered stable.

Language: Only Chinese or English.

Country(ies) involved: China.

Keywords: acupuncture, Chinese herbal medicine, insomnia, meta-analysis, protocol.

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