INPLASY PROTOCOL

To cite: Zhu et al. Acupuncture and flunarizine for migraine: A protocol for systematic review and Bayesian network meta-analysis. Inplasy protocol 202270064. doi: 10.37766/inplasy2022.7.0064

Received: 12 July 2022

Published: 12 July 2022

Corresponding author:
Zhu Wenyan

zhuwenyanamm@163.com

Author Affiliation:
Longhua Hospital, Shanghai University of Traditional Chinese Medicine.

Support: **(SHDC2020CR3091B).**

Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

Acupuncture and flunarizine for migraine：A protocol for systematic review and Bayesian network meta-analysis

Zhu, WY[1]; Pei, J[2].

Review question / Objective: **This study protocol plans to compare the efficacy and safety of acupuncture and flunarizine for migraine.**
Condition being studied: **Migraine is the most common neurovascular disease worldwide, afflicting more than one billion people worldwide . According to data from the 2019 Global Burden of Disease, Injury and Risk Factor Study, migraine is the second leading cause of disability, and as one of the parameters of "years lived with disability", it ranks first among people under the age of 50, and This brings huge economic and social burdens. Migraine is characterized by moderate or severe headache attacks with reversible neurological and systemic symptoms, such as phonophobia, nausea, and vomiting. There is sufficient evidence for the preventive treatment of migraine with flunarizine, and it is a class A recommended drug in the multinational guideline for migraine prevention. At present, the treatment methods for migraine with anxiety disorders are limited, and most patients suffer from recurrent disease, drug abuse and drug dependence. Acupuncture for the prevention and treatment of migraine has been listed by the World Health Organization as a recommended therapy for migraine treatment. Under this influence, in 2011, the Chinese Medical Association issued the guidelines for the diagnosis and treatment of migraine in China, and in 2016, it was updated to the guidelines for the prevention and treatment of migraine in China. At present, there have been many standardized clinical trials and mechanism studies to illustrate the efficacy of acupuncture and moxibustion in the treatment of migraine from different perspectives.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 July 2022 and was last updated on 12 July 2022 (registration number INPLASY202270064).

INTRODUCTION

Review question / Objective: **This study protocol plans to compare the efficacy and safety of acupuncture and flunarizine for migraine.**

Rationale: Databases including PubMed, Web of Science, Embase, Cochrane Library, Medline, China National Knowledge Infrastructure (CNKI), and Wanfang Database from their inception to 1 July 2022. Randomised controlled trials (RCTs) assessing the effectiveness of acupuncture therapy or flunarizine on the management of migraine will be selected. The outcomes are migraine frequency, migraine days, headache intensity (measured by the Visual Analogue Scale or other scales). Reviewers will conduct study selection, data extraction and risk of bias assessment procedures. Then, standard pair-wised meta-analysis and Bayesian network meta-analysis will be performed (if applicable). The Confidence in Network Meta-Analysis application will be used to assess the confidence in the evidence for the outcomes.

Condition being studied: Migraine is the most common neurovascular disease worldwide, afflicting more than one billion people worldwide . According to data from the 2019 Global Burden of Disease, Injury and Risk Factor Study, migraine is the second leading cause of disability, and as one of the parameters of "years lived with disability", it ranks first among people under the age of 50, and This brings huge economic and social burdens. Migraine is characterized by moderate or severe headache attacks with reversible neurological and systemic symptoms, such as phonophobia, nausea, and vomiting. There is sufficient evidence for the preventive treatment of migraine with flunarizine, and it is a class A recommended drug in the multinational guideline for migraine prevention. At present, the treatment methods for migraine with anxiety disorders are limited, and most patients suffer from recurrent disease, drug abuse and drug dependence. Acupuncture for the prevention and treatment of migraine has been listed by the World Health Organization as a recommended therapy for migraine treatment. Under this influence, in 2011, the Chinese Medical Association issued the guidelines for the diagnosis and treatment of migraine in China, and in 2016, it was updated to the guidelines for the prevention and treatment of migraine in China. At present, there have been many standardized clinical trials and mechanism studies to illustrate the efficacy of acupuncture and moxibustion in the treatment of migraine from different perspectives.

METHODS

Search strategy: Databases including PubMed, Web of Science, Embase, Cochrane Library, Medline, China National Knowledge Infrastructure (CNKI), and Wanfang Database from their inception to 1 July 2022. Comprehensive retrieval will be performed in the PubMed, Web of Science, Embase, Cochrane Library, Medline, China National Knowledge Infrastructure (CNKI), and Wanfang Database from their inception to 1 July 2022. No language and publication status restriction will be set in the search. In addition, reference lists of the retrieved articles will be retrospectively reviewed for potentially eligible RCTs. The following keywords or Mesh terms in combination will be used in search strategy: “randomized controlled trial” “migraine” “headache” “acupuncture” “acupuncture therapy” “flunarizine”. We will use different retrieval strategies according to the characteristics of different databases, the detailed search strategy for PubMed is shown in Table 1. We will hand-search Google Scholar (https://scholar.google.com) for relevant trials that may be missed while searching the databases.

Participant or population: For patients diagnosed with migraine according to International Classification of Headache Disorders (ICHD) developed by the International Headache Society (IHS). Migraine with aura, migraine without aura, and chronic migraine are included.

Intervention: Experimental interventions are limited to acupuncture and flunarizine. Acupuncture therapy includes related acupoint stimulations such as needle, electricity, heat, and so on.

Comparator: Control interventions include flunarizine, acupuncture, shame devise, placebo interventions, and health education.

Study designs to be included: Only randomized controlled trails will be included, whether blind or not. Languages, regions and publication status are not limited. Full text should be available and contains insufficient data for meta-analysis.

Eligibility criteria: Reviews, conference papers, animal studies, basic research, duplicate publications will be excluded. To ensure the credibility of the findings, any study with participates less than 10 will be excluded, since it may arouse potentially high risk of publication bias and influence inflated magnitude of oddsratio(OR).

Information sources: Information from PubMed, Web of Science, Embase, Cochrane Library, Medline, China National Knowledge Infrastructure (CNKI), and Wanfang Database .The lack of information should be supplemented by contacting the author.

Main outcome(s): The main outcomes will be migraine episodes and headache intensity. RCTs assess at least one of the following outcomes: migraine frequency, migraine days, headache intensity (measured by the Visual Analogue Scale or other scales).

Additional outcome(s): If some related information such as six-items headache impact test, migraine disability assessment, sleep quality assessment, mood scale and so on, show the potential value and far-reaching significance of statistical analysis, will be analyzed in future.

Data management: Two reviewers will independently extract data from eligible studies using standardized data extraction forms. The following information will be included: basic information: title, first author, publication year, country; trial design: randomization, blinding, allocation concealment; baseline characteristics of participants: sample size, gender, age, migraine type and so on; intervention: name of specific intervention, course of treatment, drug dosage; outcome measures: total clinical efficiency, symptom score, and adverse events. For multi-arm studies comparing different types of acupuncture interventions, data will be extracted for all relevant arms.

Quality assessment / Risk of bias analysis: Two reviewers will evaluate the risk of bias of all filtered trails using the Cochrane Handbook's Risk of Bias Tool for RCTs, and the third reviewer will settle disputes. For each trail, six items, including randomization process, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, missing outcome data, selective reporting, and other bias, will be evaluated respectively. The trial will be rated high, unclear or low risk of bias according to each domain.

Strategy of data synthesis: Review Manager 5.3 (Cochrane Collaboration, http://tech.cochrane.org/home) will be used to perform the pairwise meta-analysis. We estimated the summary effect size by using OR for dichotomous variables, the mean difference (MD) for continuous variables. The 95% confidence intervals (CI) will be used to indicate whether the effect index is statistically significant. The χ^2 test and I^2 test will be used to analyze the heterogeneity. We will use the network plot generated by Stata V.15.1 to compare multiple interventions simultaneously, where an intervention is represented by a node and each line between two nodes represents a direct comparison between two interventions. Node and line sizes are proportional to the number of included studies. Studies not connected to the network will be excluded from the network meta-analysis. We will perform network meta-analyses using a Bayesian framework via the "gemtc" package and "rjags" package of the R software version 4.0.4 (R Development Core Team).

Subgroup analysis: In the case of $P>0.05$ and $I^2<50\%$, multiple studies of the same type is considered to be homogeneous, adopt the fixed-effects model to calculate the combined statistics. Otherwise, a random-effects model will be adopted. If the I^2 value is greater than 75%, indicating high heterogeneity and no major source of heterogeneity identified, we will provide a narrative summary without data synthesis.

Sensitivity analysis: Sensitivity analysis involving deleting each study separately was carried out in order to assess the quality and consistency of the results and explore the robustness of the findings regarding the study quality and sample size.

Language: Languages, regions and publication status are not limited.

Country(ies) involved: China.

Keywords: Acupuncture; Flunarizine; Migraine; Systematic review;Bayesian network meta-analysis.

Contributions of each author:

Author 1 - ZHU Wenyan - searche the literature, conducte the statistical analysis, and draft the manuscript.
Email: zhuwenyanamm@163.com
Author 2 - PEI Jian - Jian Pei conceive this study.
Email: longhuaacup@aliyun.com