INPLASY PROTOCOL

Corresponding author:
Jilin Wang

wangjilin0077@163.com

Author Affiliation:
Shandong University of Traditional Chinese Medicine.

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None declared.

Comparing the efficacy and safety of traditional Chinese medicine external treatment for postherpetic neuralgia: A protocol for systematic review and network meta-analysis

Wang, J[1]; Cui, Y[2]; Liu, S[3]; Zhou, J[4]; Sun, Y[5].

Review question / Objective: The aim of this systematic review and network meta-analysis is to assess the efficacy and safety of different types of traditional Chinese medicine external treatments for postherpetic neuralgia, so as to provide comprehensive evidence for the selection of the optimal traditional Chinese medicine external treatments in the clinical treatment of postherpetic neuralgia.

Information sources: The following databases will be searched, including 4 English databases: PubMed, EMBASE, Cochrane Library, Web of Science and 4 Chinese databases: China National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Science Journal Database (VIP) and China Biology Medicine (CBM). The search time is from the establishment of each database to June 2021. A mixture of MeSH terms and free words were used to perform the search.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 June 2021 and was last updated on 21 June 2021 (registration number INPLASY202160072).

INTRODUCTION

Review question / Objective: The aim of this systematic review and network meta-analysis is to assess the efficacy and safety of different types of traditional Chinese medicine external treatments for postherpetic neuralgia, so as to provide comprehensive evidence for the selection of the optimal traditional Chinese medicine

external treatments in the clinical treatment of postherpetic neuralgia.

Rationale: Eight databases will be searched, including PubMed, EMBASE, Cochrane Library, China National Knowledge Infrastructure, Wanfang Database, Chinese Science Journal Database and China Biology Medicine from the establishment of each database to June 2021. Data will be extracted by two researchers independently according to the eligibility criteria. Statistical analysis was performed using Stata 15.0 and ADDIS 1.16.6 software. The results of this study will compare the efficacy and safety of different types of traditional Chinese medicine external treatments for postherpetic neuralgia, and rank the different types of traditional Chinese medicine external treatments according to their effectiveness.

Condition being studied: Postherpetic neuralgia is the most common complication and sequela of herpes zoster. postherpetic neuralgia was defined as chronic and solid neuropathic pain for ≥3 months after the herpes zoster rash dissipated. According to epidemiological studies, the annual incidence of PHN is 3.9-42.0/100,000 person-years. It is found that 9% to 34% of patients with herpes zoster develop postherpetic neuralgia, and the frequency and severity of postherpetic neuralgia increase with age. Current guidelines recommend treatment of postherpetic neuralgia in a hierarchical manner, with antiepileptics (gabapentin and pregabalin), tricyclic antidepressants (nortriptyline and desipramine), or topical lidocaine 5% patch as first-line drugs. However, antiepileptic drugs may cause adverse events, including dizziness, somnolence, headache. In addition, tricyclic antidepressants will bring dry mouth, weight gain, drowsiness. Furthermore, topical lidocaine patches may cause erythema, dermatitis and other application-site reactions. traditional Chinese medicine external treatment mainly includes acupuncture, moxibustion, bloodletting, cupping, plum-blossom needle, plaster and massage. In recent years, traditional Chinese medicine external treatment has been widely used in clinical and experimental studies of postherpetic neuralgia, and its effectiveness has been fully proved. However, there is still a lack of clear comparative study between various traditional Chinese medicine external treatment given the large variety of traditional Chinese medicine external treatment and the different efficacy.

METHODS

Search strategy: The following databases will be searched, including 4 English databases: PubMed, EMBASE, Cochrane Library, Web of Science and 4 Chinese databases: China National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Science Journal Database (VIP) and China Biology Medicine (CBM).The search time is from the establishment of each database to June 2021. A mixture of MeSH terms and free words were used to perform the search. Meanwhile, researchers will search for trials that are Unpublished, including Chinese Clinical Trial Registry and the US National Institutes of Health Ongoing Trials Register.

Participant or population: Patients were expected to have passed the acute stage and to be diagnosed with postherpetic neuralgia. No restrictions on age, gender and race.

Intervention: Different forms of traditional Chinese medicine external treatments, Including acupuncture, moxibustion, electroacupuncture, warming needle moxibustion, fire needle, bloodletting, cupping, plum-blossom needle, acupuncture catgut embedding, plaster and massage, etc.

Comparator: The control group was treated with Western medicine only.

Study designs to be included: All randomized controlled trial studies of traditional Chinese medicine external treatments for postherpetic neuralgia will

be included. The language of the trials to be included only Chinese or English.

Eligibility criteria: 1. Types of studies. All randomized controlled trial (RCT) studies of traditional Chinese medicine external treatments for postherpetic neuralgia will be included. The language of the trials to be included only Chinese or English. 2. Types of participants. Patients were expected to have passed the acute stage and to be diagnosed with postherpetic neuralgia. No restrictions on age, gender and race. 3. Interventions and comparisons. Different forms of traditional Chinese medicine external treatments, Including acupuncture, moxibustion, electroacupuncture, warming needle moxibustion, fire needle, bloodletting, cupping, plum-blossom needle, acupuncture catgut embedding, plaster and massage, etc. The control group was treated with Western medicine only. 4. Outcomes. (1) The primary outcome. 1. Pain intensity, measured by Visual Analogue Scale (VAS), Numerical Rating Scale (NRS), or other rating scales; 2. Recovery span of skin damage; 3. The duration of the pain. (2) The secondary outcome. 1. Quality of life asses.

Information sources: The following databases will be searched, including 4 English databases: PubMed, EMBASE, Cochrane Library, Web of Science and 4 Chinese databases: China National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Science Journal Database (VIP) and China Biology Medicine (CBM).The search time is from the establishment of each database to June 2021.A mixture of MeSH terms and free words were used to perform the search.

Main outcome(s): 1. Pain intensity, measured by Visual Analogue Scale (VAS), Numerical Rating Scale (NRS), or other rating scales; 2. Recovery span of skin damage; 3. The duration of the pain.

Additional outcome(s): 1.Quality of life assessed by the 36-Item Short-Form Health Survey (SF-36); 2. Sleep quality measured by the Pittsburgh Sleep Quality Index (PSQI); 3. Hamilton Anxiety Scale (HAMA).

Data management: All searched studies will be imported into Endnote X9.Two researchers will independently screen the studies according to the eligibility criteria. If there is a disagreement, the third researcher would make the final determination. After then, Data extraction will be performed independently by two researchers and included the following data: author's name, year of publication, title, country, average age, gender, study design, the total number of cases, participants, intervention measures, comparison, outcome, and any other relevant information. If necessary, we will try to contact the original author for unclear information.

Quality assessment / Risk of bias analysis: Two independent researchers used the Cochrane Risk of Bias Risk Assessment Tool to evaluate the quality of the study. The risk of bias in included studies will be evaluated according to 7 aspects: random method, assignment concealment, blind method of subjects, blind method of result evaluation, data integrity, selective report, and other bias. According to the quality of the included study, each evaluation indicator has 3 qualities: low risk, high risk, and unclear risk. If there are differences, they will be resolved through discussion or assistance by a third researcher.

Strategy of data synthesis: Statistical analysis was performed using Stata 15.0 and ADDIS 1.16.6 software. Stata 15.0 software was used to draw network diagrams and funnel plots. ADDIS 1.16.6 software based on the Bayesian framework was used for network meta-analysis. The effect values of dichotomous data were represented by odd ratio (OR), the effect values of continuous variables were represented by mean different (MD), and the results of statistical analysis were represented by 95% confidence interval (CI). The Markov Chain-Monte Carlo (MCMC) fitting consistent model was used to to a priori and evaluate. Four chains were used for simulation, the number of

iterations was set as 50,000. The convergence of network meta is tested using potential scale reduced factor (PSRF). When the PSRF value is closer to 1, the better the convergence result, the better the consistency model, the more credible the conclusion. The results are sorted according to Bayesian statistical methods, and the probability of interventions becoming the best treatment is determined based on the surface under the cumulative ranking.

Subgroup analysis: We will consider subgroups such as types of intervention.

Sensitivity analysis: If necessary, when each of these studies is excluded, the remaining studies will be reanalyzed to verify the stability of the results. If the qualitative change in the combined effect is not observed, it can be indicated that the results are stable.

Language: Only Chinese or English.

Country(ies) involved: China.

Keywords: traditional Chinese medicine external treatment, postherpetic neuralgia, network meta-analysis, protocol.

Contributions of each author:
Author 1 - Jilin Wang - Conceptualization; Data curation; Investigation; Software; Writing – original draft; Writing – review & editing.
Email: wangjilin0077@163.com
Author 2 - Yanru Cui - Conceptualization; Data curation; Literature retrieval; Software; Supervision; Writing – original draft; Writing – review & editing.
Email: 429731354@qq.com
Author 3 - Shuang Liu - Literature retrieval; Writing – original draft.
Email: 17862967901@163.com
Author 4 - Jiangxue Zhou - Literature retrieval; Writing – original draft.
Email: zjx971117@163.com
Author 5 - Yingxia Sun - Conceptualization; Funding acquisition; Supervision; Writing – original draft; Writing – review & editing.
Email: sunyx75@126.com