INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Comparative efficacy and Safety of Chinese patent medicine for Neck Pain: A protocol for systematic review and network meta-analysis

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Review question / Objective: **Neck Pain(NP) is a major public health concern causing chronic disability, which seriously affects people's quality of life and brings a heavy burden to families and society. Chinese patent medicine(CPM) is a patent prescription of traditional Chinese medicine (TCM),a large number of clinical studies have shown that CPM seems to be clinically effective in treating NP. However, no systematic reviews or network meta-analyses (NMA) were conducted on the topic.Therefore, this study aims to evaluate the CPM's clinical efficacy and safety for NP by performing a systematic review and network meta-analysis.**
Information sources: **This study will employ RCTs which were published in Chinese and English to assess the efficacy and safety of CPM for NP, regardless of any blind restrictions. Letters, descriptive studies, reviews, cohort studies, conference abstracts, case series, retrospective clinical studies, animal studies, case reports, protocols, cross-over studies, reports with incomplete data, studies unrelated to CPM and NP will be excluded. For any duplicate studies, only the most informative and complete report will be selected.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 March 2022 and was last updated on 13 March 2022 (registration number INPLASY202230056).

INTRODUCTION

Review question / Objective: **Neck Pain(NP) is a major public health concern causing chronic disability, which seriously affects people's quality of life and brings a heavy burden to families and society. Chinese patent medicine(CPM) is a patent prescription of traditional Chinese medicine (TCM),a large number of clinical studies have shown that CPM seems to be clinically effective in treating**

NP. However, no systematic reviews or network meta-analyses (NMA) were conducted on the topic. Therefore, this study aims to evaluate the CPM's clinical efficacy and safety for NP by performing a systematic review and network meta-analysis.

Condition being studied: Not reported.

METHODS

Search strategy: Two researchers independently and comprehensive searched will be conducted in PubMed, Web of Science(WoS), Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang Database (WANFANG),VIP Database (VIP), and Chinese Biomedical Database (CBM), from their inceptions their inception until Mar 2022. In addition, we will also perform a comprehensive search of clinical trials registries (Clinicaltrials. gov, Chinese Clinical Trial Registry, and International Clinical Trials Registry Platform) for any missed RCTs. Search terms include Neck Pain, CPM, RCTs, and their different synonyms, near-synonyms, spellings, and acronyms for each identified keyword and index term. Our search strategy consisted of Medical Subject Heading (MeSH) and free text terms.

Participant or population: The enrolled participants (18 years or older) had to be diagnosed definitely with NP and no restrictions on sex, region, nation, and duration of illness.

Intervention: In the experimental group, any form of CPM will be included, such as oral liquid, powder, tablet, pill, paste, and capsule.

Comparator: Those studies will also be included. Control interventions can be blank control, placebo control or other conventional pharmacotherapy (eg, NSAIDs, analgesics drugs, muscle relaxant drugs, and so on).

Study designs to be included: Study registration;Eligible criteria;Search strategy.Study Data extraction.

Eligibility criteria: Types of studies. This study will employ RCTs which were published in Chinese and English to assess the efficacy and safety of CPM for NP, regardless of any blind restrictions. Letters, descriptive studies, reviews, cohort studies, conference abstracts, case series, retrospective clinical studies, animal studies, case reports, protocols, cross-over studies, reports with incomplete data, studies unrelated to CPM and NP will be excluded. For any duplicate studies, only the most informative and complete report will be selected. 2.2.2. Types of participants. The enrolled participants (18 years or older) had to be diagnosed definitely with NP and no restrictions on sex, region, nation, and duration of illness. 2.2.3. Type of interventions and comparisons. In the experimental group, any form of CPM will be included, such as oral liquid, powder, tablet, pill, paste, and capsule. And there were no restrictions on dosage, duration, frequency, and administration of CPM.Considering that clinicians may combine CPM with conventional pharmacotherapy (western medicine), those studies will also be included. Control interventions can be blank control, placebo control or other conventional pharmacotherapy (eg, NSAIDs, analgesics drugs, muscle relaxant drugs, and so on). In addition, we will exclude studies involving a combination of more than two kinds of CPM. 2.2.4. Types of outcomes. The primary outcomes will consist of visual analog scale (VAS), Neck Disability Index (NDI), cure rate, and total effective rate. The incidence and severity of adverse events will be selected as a secondary outcome.

Information sources: This study will employ RCTs which were published in Chinese and English to assess the efficacy and safety of CPM for NP, regardless of any blind restrictions.Letters, descriptive studies, reviews, cohort studies, conference abstracts, case series, retrospective clinical studies, animal studies, case

reports, protocols, cross-over studies, reports with incomplete data, studies unrelated to CPM and NP will be excluded. For any duplicate studies, only the most informative and complete report will be selected.

Main outcome(s): The primary outcomes will consist of visual analog scale (VAS), Neck Disability Index (NDI), cure rate, and total effective rate. The incidence and severity of adverse events will be selected as a secondary outcome.

Quality assessment / Risk of bias analysis: We will use the current Grades of Recommendations Assessment Development and Evaluation (GRADE) guidance to assess the quality of evidence. According to the GRADE criteria, the quality of the evidence is categorized into4 classes (high, medium, low, and very low).If necessary, the comparison-adjusted funnel plot and Egger's test will be assessed for the potential publication bias. [18]In the funnel plots, if the points representing the included studies are evenly distributed, it means that the publication bias is small.

Strategy of data synthesis: NMA will be performed by Software of WinBUGS (version 1.4.3), Addis (version 1.16.8), and STATA (version 15.0). A random-effects model will be employed because of the anticipated clinical between-study heterogeneity. OR with 95% CI will be applied for dichotomous variables outcomes, while MD or SMD with 95% CI will be estimated for continuous outcomes. We will use the Brooks-Gelman-Rubin statistical method to assess the convergence of iterations. A potential scale reduction factor (PSRF) closer to 1 indicates better convergence. For the inconsistency test, we will performe node-splitting assessments to explore the association between direct and indirect evidence. Besides, to rank the size effect of treatments, surface under the cumulative ranking curve (SUCRA) value will be applied, the SUCRA values of 100% and 0% indicates the best and worst treatments.

Subgroup analysis: If the heterogeneity or inconsistency was present among the included studies, a subgroup analysis will be performed. Subgroup analysis was conducted according to the sample size, types of conventional pharmacotherapy (western medicine), treatment duration, treatment course, dosage, and other relevant parameters of included patients.

Sensitivity analysis: If feasible, we will also use the sensitivity analysis to explore the stability of the findings, and low-quality samples will be excluded.

Language: Chinese and English.

Country(ies) involved: China.

Keywords: Chinese patent medicine; neck pain; network meta-analyses; protocol.

Dissemination plans: The results of this protocol will be published in an international peer-reviewed journal, it will find out which CPM therapy has the best efficacy and safety in NP. We will update the protocol when supplements are required.

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