INPLASY PROTOCOL

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The authors declare that there is no conflict of interest regarding the publication of this paper.

The long-term efficacy comparison of five external treatments of Traditional Chinese Medicine on knee osteoarthritis: a protocol for network meta-analysis

Li, S[1]; Hu, W[2]; Wu, Q[3].

Review question / Objective: **The aim of this network meta-analysis is to synthesize and assess the long-term effectiveness and safety of external treatments of Traditional Chinese Medicine (TCM) for knee osteoarthritis (KOA) during follow-ups.**
Condition being studied: **Knee osteoarthritis (KOA) refers to a common kind of chronic inflammatory motor system disease characterized by symptoms of joint pain, articular cartilage thinning, bone loss, varied degrees of functional limitations combined with reduced quality of living. The first-line drugs used to treat KOA are nonsteroidal anti-infammatory drugs (NSAIDs). But NSAIDS has high risk for acquiring severe side effects in cardiovascular and gastrointestinal systems. Thus, alternative medical methods have become another popular way. Recent studies have showed that the external treatments of Traditional Chinese Medicine (TCM) are wildly used in managing KOA. The goals of above treatments can be concluded as the following aspects. One is the immediate effect obtained in relieving pain, stiffness and disability of KOA. The other is the long-term effect of mitigating the repercussion especially the chronic pain. However, current attention seems to be placed more in studying the immediate effects. There are few researches focusing on the long-term effects achieved by external treatments of TCM during follow-ups and the adverse events affecting patients' compliance. Direct comparisons of randomized controlled trials between different treatments are lacking. Meanwhile, some findings are suspicious in whether acupuncture methods can achieve long-term efficacy or not and the exact period of follow-up.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 July 2020 and was last updated on 28 July 2020 (registration number INPLASY202070122).

INTRODUCTION

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METHODS

Search strategy: Electronic Databases: PubMed, EMbase, the Cochrane Library, China Biology Medicine (CBM), China National Knowledge Infrastructure (CNKI), WanFang Database, VIP Database. Search Terms and Strategy: #1 "Osteoarthritis, Knee"[MeSH] #2 "Knee Osteoarthritides" #3 "Knee Osteoarthritis" #4 "Osteoarthritides, Knee" #5 "Osteoarthritis Of Knee" #6 "Knee, Osteoarthritis Of" #7 "Knees, Osteoarthritis Of" #8 "Osteoarthritis Of Knees" #9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 #10 "Medicine, Chinese Traditional"[MeSH] #11 "Traditional Chinese Medicine" #12 "Chung I Hsueh" #13 "Hsueh, Chung I" #14 "Traditional Medicine, Chinese" #15 "Zhong Yi Xue" #16 "Chinese Traditional Medicine" #17 "Chinese Medicine, Traditional" #18 "Traditional Tongue Diagnosis" #19 "Tongue Diagnoses, Traditional" #20 "Tongue Diagnosis, Traditional" #21 "Traditional Tongue Diagnoses" #22 "Traditional Tongue Assessment" #23 "Tongue Assessment, Traditional" #24 "Traditional Tongue Assessments" #25 #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 #26 "Randomized Controlled Trial as Topic"[MeSH] #27 "Clinical Trials, Randomized" #28 "Trials, Randomized Clinical" #29 "Controlled Clinical Trials, Randomized" #30 #26 OR #27 OR #28 OR #29 #31 #9 AND #25 AND #30.

Participant or population: Patients with a diagnosis of knee osteoarthritis (KOA). There are no restrictions of age, sex, course of disease, race, etc.

Intervention: Intervention of treatment group was restricted with only one external treatments of TCM.

Comparator: Intervention of control group was another external treatment of TCM different from that of the treatment group.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: (1) Studies were randomized controlled trials (RCTs). (2) Patients were diagnosed with KOA. (3) Intervention of treatment group was restricted with only one external treatments of TCM while that of control group was another external treatment of TCM. (4) There are records of follow-ups. (5) The outcome indicator was Western Ontario and McMaster Osteoarthritis Index (WOMAC) scores.

Information sources: Chinese Database: China Biology Medicine, China National Knowledge Infrastructure (CNKI), Wanfang

Data, VIP database; English Database: Pubmed, Cochrane Library, EMbase.

Main outcome(s): Western Ontario and McMaster Osteoarthritis Index (WOMAC) scores.

Additional outcome(s): N/A.

Quality assessment / Risk of bias analysis: Two authors will assess the risk of bias of the included studies using the methods recommended by the Cochrane Collaboration for the following terms. Six domains should be scored: sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting and other sources of bias. The risk of bias was graded as low, high and unclear.

Strategy of data synthesis: All data analyses will be conducted by Review Manager Software Version 5.3 and Stata Version 15.1/SE. A network meta-analysis with a frequentist approach using the Review Manager Software Version 5.3 and Stata Version 15.1/SE. According to the P value of firstly used global inconsistency model, the model type will then be decided to be consistency or inconsistency. Additionally, local inconsistency will be tested by using the node-split model. If the P value tested in global and local inconsistency model are both more than 0.05, the consistency model can be used for the following analysis. Otherwise, the statistics should be performed and explained with inconsistency model. Comparisons of effectiveness among single external treatments of TCM can be embodied in ranking probability with surface under the cumulative ranking curve (SUCRA). Meanwhile, the valid comparisons can be seen in the league table. If the 95% CI of one study is not contain value 0, it is generally believed that there exist differences in efficacy between the two treatments. The results will be embodied in network graph, forest plot, SUCRA, league table and the publication bias graphs.If the evidence included cannot support a network meta-analysis, a original meta-analysis will be done. Mean difference (MD) and 95% confidence intervals (CIs) will be used for continuous outcome.

Subgroup analysis: Network meta-analysis does not need subgroup analysis.

Sensibility analysis: Network meta-analysis does not need sensibility analysis.

Country(ies) involved: China.

Keywords: Osteoarthritis of the Knee; Network Meta-Analysis; External Treatments of Traditional Chinese Medicine; Efficacy Comparison.

Contributions of each author:
Author 1 - Sihui Li - Author 1 drafted the manuscript.
Author 2 - Weishang Hu - Author 2 contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 3 - Qiaofeng Wu - Author 3 checked the manuscript.