The effects of electroacupuncture in treatment of knee osteoarthritis: A protocol for meta-analysis of randomized controlled trials

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Review question / Objective: The purpose of this meta-analysis was to evaluate the comparative efficacy of EA and medication in the management of KOA pain and knee function recovery, particularly the role of EA in the treatment of KOA.

Condition being studied: Knee osteoarthritis (KOA) is a common chronic joint disease which based on degenerative joint disorders that cause pain and limitation of function and may be the leading cause of disability in adults. Pain caused by KOA is an important outcome in the progression of the disease, which may...

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Conflicts of interest: None declared.
result in brain structural and organizational changes, limit the patient's mobility, and cause difficulty in performing daily activities and participating in social events. Therefore, the current treatment of KOA is mainly aimed at reducing joint pain and slowing its progression. The latest guidelines for nonsurgical management of knee osteoarthritis include arthritis education and structured land-based exercise programs with or without dietary weight management, non-pharmacological and pharmacologic management. Pharmacologic therapy is also widely used, including paracetamol, oral non-steroidal anti-inflammatory drugs (NSAIDs), opioids, oral symptomatic slow-acting drugs for osteoarthritis (SYSADOAs), and off-label prescription of duloxetine. However, pharmacologic therapy may have some adverse effects such as addiction and damage to renal system and gastrointestinal tract, so there are certain limitations in clinical application. KOA's guidelines are for a more conservative, non-pharmacological approach to managing chronic knee pain that is central to achieving similar or better outcomes at a lower cost than pharmacotherapy. Acupuncture, as a non-drug treatment, is one of the most popular alternative therapies in medicine and is often used and effective in treating patients with chronic pain, including joint pain, in the United States. Electroacupuncture (EA) combines traditional acupuncture, which has been used for decades, by connecting electrodes to pairs of needles for electrical stimulation. One study showed that EA produced greater analgesia for different types of pain than manual acupuncture (MA). In addition, some researchers believe that EA and MA have different analgesic mechanisms and therefore need to be studied separately. Compared with traditional acupuncture or MA, EA needs more attention in KOA analgesia. However, different KOA guidelines are controversial regarding the use of acupuncture/EA, mainly because they do not separate traditional acupuncture and EA in terms of treatment. EA and pharmacologic treatments are both widely used treatments, but there is still controversy over the best intervention for pain control in knee osteoarthritis. Meta-analysis is a relatively new method of evidence generation that combines all direct or indirect evidence from different treatment comparisons, enabling uniform and coherent analyses of all trials. Although some meta-analyses have been conducted to verify the conclusion that fire acupuncture is superior to EA, fire acupuncture is superior to drugs, and EA is superior to conventional treatment, there is no relevant review and meta-analysis on the effectiveness of EA and pharmacologic treatments in treating KOA.

METHODS

Search strategy: We will electronically search the following four international and four Chinese databases from 2012 to 2021: Web of Science, The Cochrane Library, PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), Wan Fang Digital Journals, SinoMed and VIP information (VIP). PROSPERO database and INPLASY database will also be searched. A combination of terms of Medical Subject Headings (MeSH) and keywords will be used in the search strategy, including KOA and EA. The search words in the Chinese databases have the same meaning as those used in the English databases. Protocols and conference reports will be excluded. There was no restriction on language.

Participant or population: Patients of any age, gender or ethnicity with a clinical diagnosis of KOA in accordance with the diagnostic criteria of standard diagnostic criteria (the Chinese Medical Association criteria or the American College of Rheumatology criteria) will be included. Patients after total knee arthroplasty will be excluded.

Intervention: The studies will be included if it: utilizes EA as the sole treatment of KOA.

Comparator: Analgesic drugs or any drugs to relieve the pain as compared control comparators.
Study designs to be included: Only randomized controlled trials (RCTs) utilizing EA against paregoric in treating patients with KOA will be included in this paper. Non-randomized clinical trials, protocols and reviews will be excluded.

Eligibility criteria: Only randomized controlled trials (RCTs) utilizing EA against paregoric in treating patients with KOA will be included in this paper. Patients of any age, gender or ethnicity with a clinical diagnosis of KOA in accordance with the diagnostic criteria of standard diagnostic criteria (the Chinese Medical Association criteria or the American College of Rheumatology criteria will be included. The studies will be included if it: utilizes EA as the sole treatment of KOA, and analgesic drugs or any drugs to relieve the pain as compared control comparators.

Information sources: We will electronically search the following four international and four Chinese databases from 2012 to 2021: Web of Science, The Cochrane Library, PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), Wan Fang Digital Journals, SinoMed and VIP information (VIP). PROSPERO database and INPLASY database will also be searched.

Main outcome(s): The effect of treatment in pain relief will be evaluated by the visual analogue scale (VAS).

Additional outcome(s): The effect of treatment in pain relief will be evaluated by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total score and WOMAC score pain subscale.

Data management: The search results from the above 8 databases will be imported to NoteExpress software to data management, and the duplicated articles will be filtered.

Quality assessment / Risk of bias analysis: According to Grading of Recommendations Assessment Development and Evaluation (GRADE), we will assess the quality of evidence as 4 levels: high quality, moderate quality, low quality, and very low quality. In addition, we will use the Guideline Development Tool (GRADEpro GDT) to conduct this process. Two researches (Peiqi Li and Yuchen Zhang) will independently evaluate the quality of the included literature mainly according to the Cochrane Collaboration’s tool for assessing risk of bias in randomized trials. The Cochrane Risk of Bias tool contains 7 specific domains: sequence generation, allocation concealment, participant and personnel blinding, outcome assessment blinding, incomplete outcome data, selective reporting, and other bias items. Two researchers will grade the above contents as “low risk”, “high risk” or “unclear”, and cross-checked the obtained results. Any conflicts or discrepancies will be solved by discussion, or a third researcher (Bin Xiao) will be consulted to achieve agreements. Finally, a bias risk diagram will be drawn using RevMan5.3 software.

Strategy of data synthesis: Tables will be produced to detail the included studies and the data extracted. In addition, we will synthesis these data to provide pooled treatment effects. The measurement data will use the mean difference (MD) as the effect indicator for continuous variables. Each effect indicator will be expressed with 95% confidence interval. Heterogeneity will be tested by I2. The heterogeneity and size of each study result will be judged using statistical methods. For studies with no statistical heterogeneity (I2 < 50%, P > 0.1), the analysis will be performed using a fixed-effect model, whereas a randomized effects model will be applied if studies have significant statistical heterogeneity.

Subgroup analysis: When sufficient data is available, we will conduct the following subgroup analysis to investigate the source of heterogeneity: waveform and KOA of different courses.

Sensitivity analysis: According to sample size, methodological quality, and the effect of missing data, when the outcome analyses involve a large degree of
heterogeneity, sensitivity analysis will be conducted to determine the impact of studies with higher risk of bias on the overall estimate of effect of the intervention, and identify the robustness of the meta-analysis result.

**Language:** There was no restriction on language.

**Country(ies) involved:** China.

**Keywords:** meta-analysis; protocol; knee osteoarthritis; electroacupuncture.

**Contributions of each author:**
Author 1 - Peiqi Li.
Author 2 - Yuchen Zhang.
Author 3 - Fanlian Li.
Author 4 - Feihong Cai.
Author 5 - Bin Xiao.