INPLASY PROTOCOL

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Conflicts of interest: None declared.

Effect of acupuncture and moxibustion on cartilage in animal model of knee osteoarthritis: a systematic review and meta-analysis

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Review question / Objective: Participants: Animals with knee osteoarthritis established by various methods. Intervention: Receiving acupuncture treatment after modeling. Comparison: Untreated animal models of knee osteoarthritis (model group). Results: The cytokines included Cysteinyl aspartate specific proteinase-1 (caspase-1), caspase-3, B-cell lymphoma-2 (Bcl-2), BCL2 associated X The levels of protein (Bax), matrix metalloproteinase-13 (MMP-13), depolymerizing protein-like metalloproteinase-5 (ADAMST-5), osteoprotegerin (OPG), receptor activator of nuclear factor-κB ligand (RANKL), Tunel cell apoptosis rate, cartilage Mankin's score, LequensneMG score, subchondral bone volume to total volume ratio (BS/TV), bone surface area/Bone volume ratio (BS/BV), average trabecular thickness (TbTh), average number of trabecular bone per unit length (TbN), and average distance between trabecular bone (cylindrical structure) (TB.sp).

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 September 2022 and was last updated on 29 September 2022 (registration number INPLASY202290125).

INTRODUCTION

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Condition being studied: In order to improve the accuracy of clinical research and master the internal mechanism of acupuncture in the treatment of knee osteoarthritis, the research of animal model of acupuncture in the treatment of knee osteoarthritis came into being. It is well known that the main pathological change of knee osteoarthritis is cartilage degeneration. After the occurrence of knee osteoarthritis, the balance between synthesis and metabolism of chondrocytes is broken, which leads to the limited secretion of extracellular matrix to maintain normal cartilage function, and finally accelerates the occurrence of cartilage destruction. We know that acupuncture can improve the apoptotic state and degree of destruction of cartilage by regulating the level of cytokines in cartilage. Therefore, it has become a major trend to study the regulation of cartilage by acupuncture and moxibustion in animal models of knee osteoarthritis.

METHODS

Participant or population: Animals with knee osteoarthritis established by various methods are not limited in species, sex, weight and age.

Intervention: Acupuncture treatment should be carried out after the model is established, with no restrictions on acupuncture methods, types, frequency, course of treatment and stimulation intensity.

Comparator: Knee osteoarthritis model group animals without intervention.

Study designs to be included: This study included animal studies of acupuncture in the treatment of knee osteoarthritis, focusing on the mechanism of effects at the cartilage level.

Eligibility criteria: Exclusion Criteria: (1) Non-simple acupunctureresearch. (2) Non-knee osteoarthritis research. (3) Animal experiments with non-randomized control design. (4) Study on non-cartilage tissue of samples submitted for examination. (5) Studies with different measurement units under each outcome indicator (which cannot be converted into eachother). (6) Review, abstract, conference paper, dissertation. (7) Repeated and dataidentical studies.

Information sources: This meta-analysis was conducted according to the PRISMA 2020 statement: an updated guidelines for reporting systematic reviews. This review does not have any preregistered protocols. two authors independently searched the databases of Pubmed, Embase, Web of science(including Medline), cochrane library Scopus CNKI Wan Fang VIP. The search time is limited to the establishment of the database until September 2022. The search terms are:acupuncture, electroacupuncture, acupoint, Osteoarthritis, Knee, Knee Osteoarthritides, Knee Osteoarthritis, Animal Model, animals. each search Word are used alone or in combination.

Main outcome(s): The cytokines included Cysteinyl aspartate specific proteinase-1 (caspase-1), caspase-3, B-cell lymphoma-2 (Bcl-2), BCL2 associated X The levels of protein (Bax), matrix metalloproteinase-13 (MMP-13), depolymerizing protein-like metalloproteinase-5 (ADAMST-5), osteoprotegerin (OPG), receptor activator of nuclear factor-kB ligand (RANKL), Tunel cell apoptosis rate, cartilage Mankin's score, LequensneMG score, subchondral bone volume to total volume ratio (BS/TV), bone surface area/Bone volume ratio (BS/ BV), average trabecular thickness (TbTh), average number of trabecular bone per unit length (TbN), and average distance between trabecular bone (cylindrical structure)(TB.sp).

Quality assessment / Risk of bias analysis:

The methodological quality of each included study was assessed by two authors using a 10-item checklist modified from the Collaborative Approach to Meta-Analysis and Review of Animal Data from **Experimental Studies (CAMARADES)** checklist: Sample size calculation: A statement describing temperature and humidity control; Randomization to treatment or control; Use a reasonable knee osteoarthritis model; Assess the success of the model; The use of anesthetics with no obvious specificity; Results Blind method; Comply with animal ethics regulations; Published in a peerreviewed journal; Declare no potential conflicts of interest.. The sum of the quality scores was recorded for each article, with a possible total score of 10 points.

Strategy of data synthesis: Review Manager 5.4 was used for statistical analysis of the data. First, the heterogeneity test was performed. When the studies were homogenous (P \geq 0.05, I2 ≤ 50%), the fixed-effects model (FE) was used for analysis. If there was significant heterogeneity among the studies (P < 0.05, 12 > 50%), a random-effects model (RE) was used for the analysis, and a sensitivity analysis was performed to examine the sources of heterogeneity and to assess the stability of the results. The outcome indicators of this study were all continuous variables, and their outcomes were expressed by standard mean difference (SMD) and 95% confidence interval (95% CI). The 95% CI did not contain 0, indicating that the results were statistically different (P < 0.05), and finally a funnel plot was used to analyze potential publication bias.

Subgroup analysis: In order to observe the effect of different acupuncture prescriptions on the results when measuring the outcomes of the mankin's score, we set up subgroups according to different acupoint combinations, acupuncture methods, and treatment

courses. Sensitivity analysis: If randomeffects model (RE) was used for the analysis, and a sensitivity analysis was performed to examine the sources of heterogeneity and to assess the stability of the results.

Sensitivity analysis: If random-effects model (RE) was used for the analysis, and a sensitivity analysis was performed to examine the sources of heterogeneity and to assess the stability of the results.

Country(ies) involved: China.

Keywords: Acupuncture; Knee osteoarthritis; Cartilage. Cytokines; Animal model; Meta analysis.

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